FORMULATION AND EVALUATION OF ACECLOFENAC MICROCAPSULES USING DIFFERENT POLYMERS

Dissertation submitted to

THE TAMILNADU Dr.M.G.R MEDICAL UNIVERSITY, CHENNAI-32

In partial fulfillment of the requirement for the award of the degree of

MASTER OF PHARMACY
IN
PHARMACEUTICS

Submitted by

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CERTIFICATE

This is to certify that the work presented in the thesis entitled **"FORMULATION AND EVALUATION OF ACECLOFENAC MICROCAPSULES USING DIFFERENT POLYMERS"** was carried out by **YOGESHWARAN. G (Reg. No. 261211451)**, in partial fulfillment of the requirement for the award of Degree of **Master of Pharmacy in Pharmaceutics** under The Tamilnadu Dr.MGR Medical University is an authentic work carried out under my direct supervision and my fullest satisfaction.

To the best of my knowledge, the content of this thesis does not form a basis for the award of any previous Degree to anyone else.

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Date:

DECLARATION CERTIFICATE

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EVALUATION CERTIFICATE

This is to certify that the work embodied in this thesis entitled "**FORMULATION AND EVALUATION OF ACECLOFENAC MICROCAPSULES USING DIFFERENT POLYMERS"** submitted to The Tamilnadu Dr. M.G.R. Medical University Chennai, was carried out by **YOGESHWARAN. G (Reg. No. 261211451)** in the **Department of Pharmaceutics**, PGP College of Pharmaceutical Science and Research Institute, Namakkal in the partial fulfillment of the Degree of **"Master of Pharmacy"** in Pharmaceutics under the supervision and guidance of **Mr. D.SAKTHIVEL, M.Pharm.,Ph.D**. Asst. Professor, Department of Pharmaceutics, PGP College of Pharmaceutical Science and Research Institute, Namakkal-637 207.

This work is original and has not been submitted in part or full for the award of any other degree or diploma of any other University.

INTERNAL EXAMINER **EXTERNAL EXAMINER**

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In this moment I thank to all my family members and friends for their selfless love, support and constant prayers, with which this work has been successful.

By

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ABSTRACT

In this dissertation work, the drug Aceclofenac is tried to micro encapsulated with two different polymers such as ethyl cellulose, polyvinyl pyrrolidone. Microcapsules were prepared by solvent evaporation method using an acetone / liquid paraffin system, in which the drug particles are dispersed in a polymeric solution which is emulsified into external phase containing emulsifier [Span 80]. For each polymer the microcapsule preparations are done in three different ratios of drug to the polymer. A key variable for successful microencapsulation was the selection of proper type and concentration of the emulsifier. The results showed that the Ethylcellose and Polyvinyl pyrrolidone are able to microencapsulate the drug. The drug-loaded microcapsules showed highest encapsulation efficiency with 1:1 drug to polymer ratio in case of Ethyl cellulose microcapsules and 1:2 ratio in case of polyvinylpyrrolidone microcapsules. The expected reason for this difference in release rate between ratios of same polymeric microcapsules was based on the particle size and size distribution of microcapsules. The infrared spectra thermographs showed stable character of Aceclofenac in drug-loaded microcapsules and revealed the absence of drug-polymer interactions. Microscopic study revealed that the Ethylcellulose microcapsules were spherical in nature and Polyvinyl pyrrolidone microcapsules were mostly irregular in nature.

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1. INTRODUCTION

An ideal dosage regimen in the drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma and maintains it constant for the entire duration of treatment. This is possible through administration of a conventional dosage form in a particular frequency and dose.[1] But the dosing interval is shorter than half-life of drug resulting in a number of limitations such as –

1. Poor patient compliance.
2. Unavoidable fluctuations in drug concentration in blood.
3. Fluctuations may lead to adverse effects especially of a drug with small therapeutic index.
4. Peak valley plasma drug level is obtained which makes attainment of steady state condition difficult.

There are two ways to overcome such a situation –

1. Development of new, better and safer drugs with long half-lives and large therapeutic indices, and
2. Effective and safer use of existing drugs in the form of controlled drug delivery systems.

The first approach has many disadvantages which therefore resulted in increased interest in the second approach. An ideal controlled drug delivery system is one which delivers the drug at a pre-determined rate, locally or systematically, for a specified period of time.

In general, controlled delivery attempts to –

1. Sustain drug action at a predetermined rate by maintaining a constant blood level of the drug.
2. Localize drug action by spatial placement of controlled released system adjacent to the diseased tissue.
3. Targeting drug action by using carriers.

There are three types of **controlled drug delivery systems**, namely

i) **Passive Preprogrammed**, in which the release rate is predetermined and is irresponsive to the external biological environment.

ii) **Active Preprogrammed**, in which the release rate can be altered by the external source.

iii) **Active self-programmed**, in which the release rate is depend on response to information, registered by a sensor, on the changing biological environment such as blood sugar level.

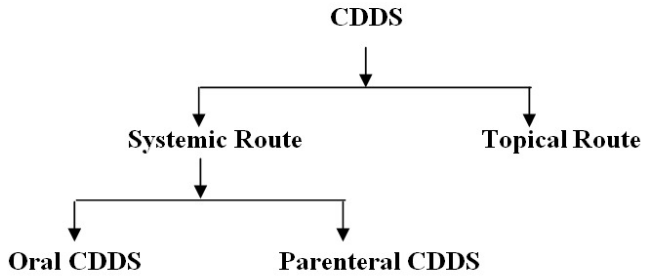
The several **advantages** of controlled drug delivering system over a conventional dosage form are –

1. Improved patient convenience and compliance.
2. Reduction in fluctuation in steady state level of drug, so therefore better control of disease.
3. Increased safety margin of highly potent drugs.
4. Maximum utilization of drugs.
5. Reduction in health care costs.

Disadvantages of control release dosage form include -

1. Decreased systemic availability due to incomplete release, increased first pass metabolism, increased instability, in sufficient resistance time for complete release, site specific absorption, etc.
2. Poor in vitro – in vivo correlation.
3. Possibility of dose dumping.
4. Retrieval of drug is difficult in case of toxicity.
5. Higher cost of formulation.

The controlled drug delivery Systems (CDDS) are mainly administered as:



Oral Ingestion has long been the most convenient and commonly employed route of drug delivery. Indeed, for sustained release system the oral route of administration has received most attention with respect to research on physiological and drug constraints as well as design and testing of products. This is because there is more flexibility in dosage form design for the oral route than these three for the parenteral route.

The following are the different oral sustained drug delivery systems:

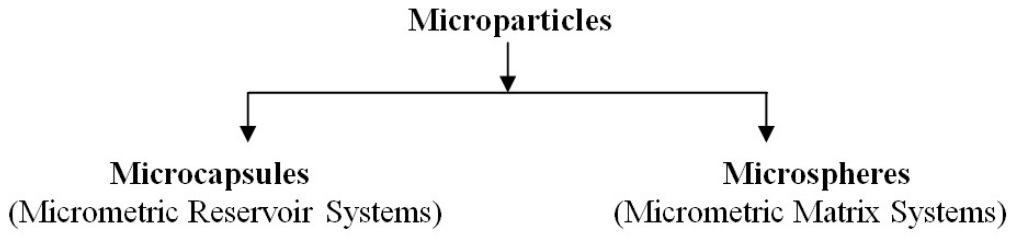
a. Dissolution control release.
b. Diffusion control release.
c. Diffusion and Dissolution control release.
d. Ion-Exchange resins.
e. pH-independent formulations.
f. Osmotically controlled release.
g. Altered density formulations.

Microencapsulation techniques are the one of the methods used to prepare the above two controlled release systems like diffusion controlled release and dissolution controlled release.

MICROPARTICLES[2]

These are the particles with size more than '1'μm, containing the polymer. At present, there is no universally accepted size range that particles must have in order to be classified as microparticles. However, many workers classify the particles smaller than '1'μm, as nanoparticles and those more than 1000 μm as macroparticles.

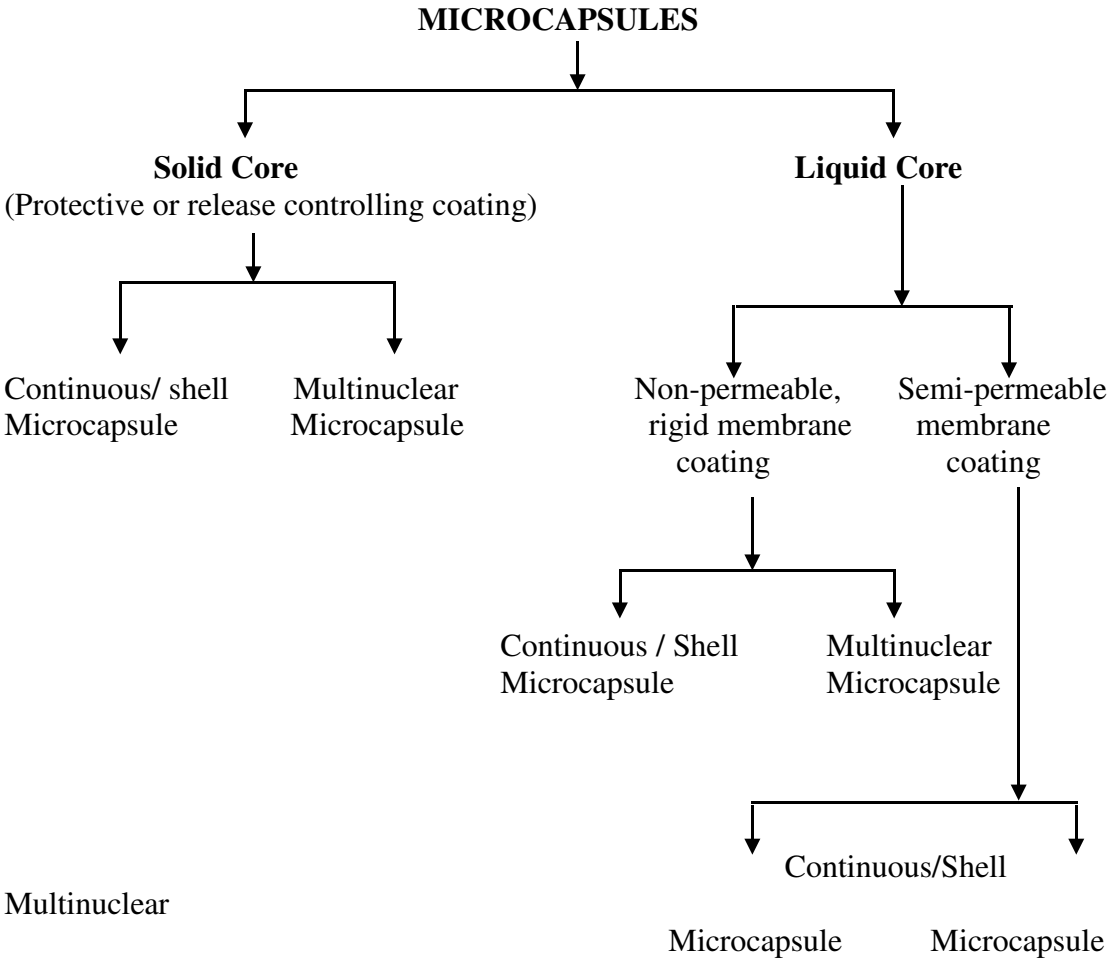
Classification – Microparticles are classified into two groups,



MICROSPHERES

Microspheres are solid, spherical particles containing dispersed drug molecules, either in solution or crystalline form, among the polymer molecules.

TYPES OF MICROCAPSULES



Microcapsules have an either spherical geometry with a continuous core region surrounded by a continuous shell or have an irregular geometry and contain a number of small droplets.

CRITERIA FOR COATING MATERIALS[3]

The coating materials should meet the following ideal criteria.

1. Capable of forming a film that is cohesive with the core material.
2. Chemically compatible and non-reactive with the core material.
3. Provide the desired coating properties such as strength, flexibility, impermeability, optical properties and stability.

METHOD OF MICROCAPSULES PREPARATION

There are two types of process to prepare microcapsules.

TYPE – A (CHEMICAL) PROCESS

1. Coacervation – Phase separation.
2. Interfacial polymerization.
3. In-situ polymerization.
4. Solvent evaporation.
5. Solvent extraction.

TYPE – B (MECHNAICAL) PROCESS

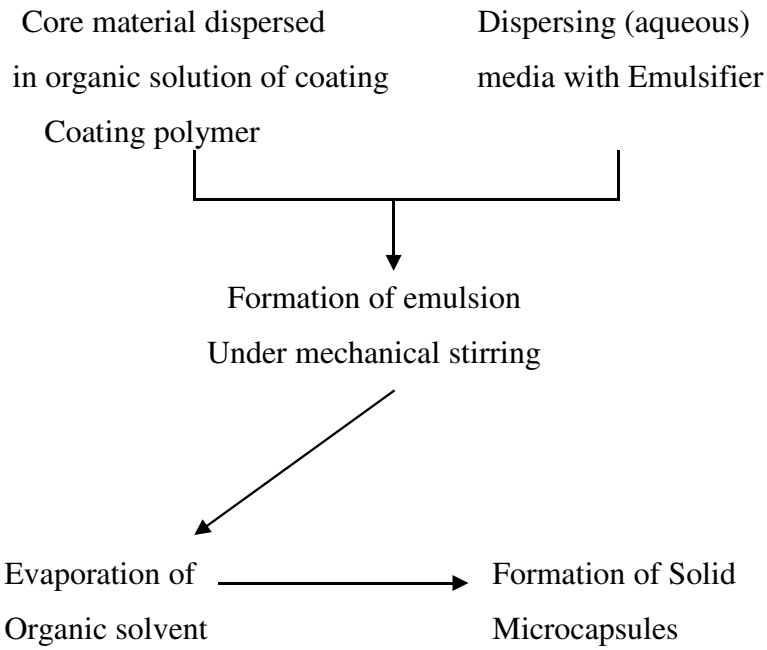
1. Spray drying.
2. Fluidized Bed coating.
3. Multiorifice – centrifugal processes.
4. Pan coating.

TYPE 'A' PROCESS

Solvent – Evaporation Method
(Emulsification – evaporation Method)

This technique is based on the evaporation of the internal phase of an emulsion by agitation. Initially, the coating polymeric material is dissolved in a volatile organic solvent. The core to be encapsulated is then dispersed in the coating polymer solution to form a suspension or emulsion.

In the next step, this organic solution is emulsified under agitation in a dispersing phase, which is immiscible with the organic solvent, which contains the emulsifier. Once the emulsion is stabilized, agitation is maintained and the solvent evaporates after diffusing through the continuous phase. This results in the formation of microcapsule. On the completion of the process, the microcapsules held in suspension in the continuous phase are recovered by filtration or centrifugation and are washed and dried.



Solvent evaporation technique is basically divided into '3' different types of techniques –

i. **Oil in Water Emulsion**

In this system, the polymer is dissolved in an organic solvent such as Dichloromethane or Chloroform. The active principle/core dispersed in the same medium and then the entire mixture is emulsified in an aqueous solution containing emulsifier.

Factors governing the Encapsulation efficiency of drug –

a. **Partition coefficient** - The partitioning phenomena operates between the dispersed and the dispersing phases which contributes to a substantial lowering of microencapsulation efficiency.
b. Degree of ionization.

Strategy for improving Encapsulation Efficiency of Drug –

a. Water solubility of the drug can be reduced by chemical modification prior to its incorporation in the organic phase.

   However, such structural modification may give rise to toxicological problems.
b. Modifying the dispersing phase of the emulsion to reduce leakage of the drug from oily droplets of polymer solution.

Modifications like,

a. Saturating the continuous phase with the drug
b. Adjusting the pH of this same phase
c. Adding the elctrolytes

However the validity and effectiveness of these strategies vary from case to case. For example, chemical modification only concern to a limited number of active substances, and the saturation of external phase is only of value for low water soluble drugs or inexpensive drugs. Similarly, if the adjusting of pH can prove advantageous for ionization drugs, this procedure generally accelerates the degradation of some polymers.

ii. **Multiple Emulsion** : **w/o/w**

In these systems, active principles to be encapsulated are incorporated in an aqueous solution, which is poured into a casting organic solution of the polymer to form an emulsion of the type w/o. This primary emulsion is itself emulsified in an external aqueous phase leading to a multiple emulsion of the type w/o/w, the organic phase acts as a barrier between the two aqueous compartments preventing the diffusion of the medicine towards the aqueous phase.

Advantage – This process is more effective when the water solubility of the drug is high and partitioning between the organic phase is disfavourable.

Application – This process is used for encapsulation of drug which are strongly water soluble.

iii. **Non-aqueous Emulsion** : **o/o emulsion**

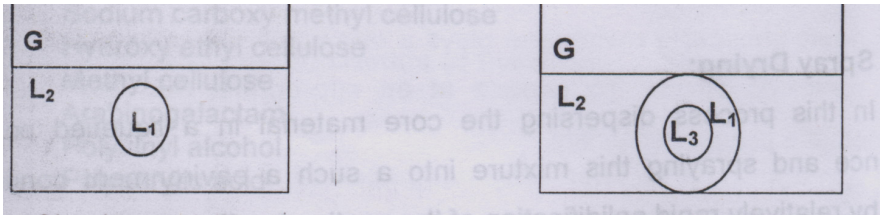
This technique is similar to o/w emulsion evaporation but dispersing medium can be constituted by a mineral or vegetable or a non-volatile organic solvent.

Advantage – This technique prevent hydrolysis of some drug

Disadvantage – This technique often expensive and need to be recycled.

Mechanism of Solvent Evaporation Method

This system is characterized by the existence of several interfaces through which mass transfer occurs during particle formation, as shown in the below in figure.



Simple Emulsion (o/w or o/o) Multiple Emulsion (w/o/w)

Figure 1

Organic solvent of the dispersed phase of the emulsion is eliminated in two stages–

1. Diffusion of the solvent in the dispersing phase
2. Elimination of the solvent at dispersing phase – air interface

The formation of solid microcapsule is brought about by the evaporation of the volatile solvent L_1 the interface L_2/G. During the course of solvent evaporation, a partitioning is produced across the interface L_1 / L_2 from the dispersed phase to continuous phase leading to the formation of solid microcapsules.

Solvent – Extraction Method

As mentioned in the previous method, the organic solvent of the dispersed phase of the emulsion is eliminated in two stages, i.e.

i. Diffusion into continuous phase, and

ii. Elimination of solvent at continuous phase – air interface

If one uses a continuous phase which will immediately extract the solvent of the dispersed phase, the evaporation stage is no longer necessary in microencapsulation.

In practice it is achieved

a. by using large volume of dispersing phase w.t.o dispersed phase. Or

b. by choosing a cosolvents in dispersed phase, of which at least one has a great affinity for the dispersing phase. Or

c. by formulating a dispersing phase with two solvents in which one acts as a solvent extractor of the dispersed phase.

TYPE 'B' PROCESSES

1. **Spray Drying**

   In this process dispersing the core material in a liquefied coating substance and spraying this mixture into such an environment condition where by relatively rapid solidification of the coating is effected.

   Advantage – Low cost of encapsulation and able to produce large amount of microcapsules.

   Disadvantage – This process is limited to coating material soluble in water, but the list of water soluble coating materials are limited.

2. **Fluidized bed coating (Wurster Air Suspension)**

   It consists of the dispersing of solid core materials in a supporting air stream and then spray coating of the air suspended particles.

   Advantage – Able to handle an extremely wide range of coating formulations.

3. **Multi orifice – Centrifugal Processes**

   In this process it utilizes centrifugal forces to hurl a core material particle through an enveloping microencapsulating membrane, thereby affecting mechanical microencapsulation.

4. **Pan Coating**

   The coating material solution is applied as a solution to the solid core material in a coating pan.

POLYMERS USED FOR MICROENCAPSULATION[3]

I. Water Soluble resins

- Gelatin
- Gum Arabic

- Starch
- Polyvinyl pyrrolidone
- Sodium carboxy methyl cellulose
- Hydroxy ethyl cellulose
- Methyl cellulose
- Arabinogalactam
- Polyvinyl alcohol
- Polyacrylic acid

II. Water Insoluble resins

- Ethyl cellulose
- Polymethyl methacrylate (PMMA)
- Polymethacrylate (Eudragit)
- Polyethylene
- Polyamide (Nylon)
- Poly (Ethylene-vinyl acetate)
- Cellulose nitrate
- Silicones
- Poly(lactide-co-glycolide)
- Cellulose acetate butyrate

III. Waxes and Lipids

- Paraffin
- Carnauba Wax
- Spermaceti
- Bees Wax
- Stearic Acid
- Stearyl Alcohol
- Glyceryl Stearates

IV. Enteric Resins

- Shellac
- Cellulose acetate phthalate
- Zein

MECHANISM OF DRUG RELEASE FROM MICROCAPSULES[4]

In the controlled release of drug from polymer-membrane permeation controlled drug delivery system, the drug particles are visualized as not being releasable from the device until the drug molecules on the outer most surface layer of a drug practice dissociate from their crystal lattice structure dissolve or partition into the surrounding polymer (in membrane), diffuse through it and finally partition into the elution medium surrounding drug delivery system.

This mechanistic analysis suggests that the solubility of a drug species in a rate-controlling membrane plays a rate controlling role in its release from a polymeric device. To release at an appropriate rate the drug requires adequate polymer solubility.

FACTOR INFLUENCING THE DESIGN OF ORAL SUSTAINED RELEASE PRODUCTS[1, 5]

A. Physicochemical Properties of Drug

i. Aqueous Solubility

Drugs with good aqueous solubility are the good candidates for oral sustained drug delivery system (SDDS). Whereas drugs with very low solubility (<0.01 mg/ml) are inherently sustained, since their release over the time course of a dosage form in the G.I.T will be limited by dissolution of drug.

ii. Partition Coefficient ($PK_{o/w}$)

Drugs with extremely high $PK_{o/w}$ readily penetrate the biological membrane but are unable to proceed further, while drugs with excessive aqueous solubility, i.e. low Pko/w cannot penetrate the membrane. Hence a balance in the $PK_{o/w}$ is needed.

iii. Drug Stability

Drugs that are unstable in the stomach can be placed in a slowly soluble form or have their release delayed until they reach the small intestine. However, such a strategy would be detrimental for drug that either unstable in the small intestine or undergo extensive gut-wall metabolism, as evidenced by reduced bioavailability when these drugs are administered from a SDDS.

iv. Protein Binding

If the drugs are having high degree of blood protein binding, then they are serve as a depot for drug producing a prolonged release profile.

B. Pharmacokinetic Characteristics of the Drug

i. Absorption

Drug for an oral SDDS its absorption rate must be efficient since the desired rate limiting step is rate of drug release K_r, i.e. $K_r << K_a$. A drug with slow absorption is a poor candidate for SDDS.

ii. Elimination of half-life

Drug with half-life in the range of 2-4 hrs make good candidates for such a system. For drugs with t ½ less than '2' hrs, a very large dose may be required to maintain the high release rate. Similarly drugs with long t ½ need to be presented in such a formulation.

iii. Metabolism

Drug which is extensively metabolized is suitable for SDDS as long as the rate of metabolism is not too rapid. A drug capable of inducing or inhibiting metabolism is a poor candidate for SDDS. Since steady state blood level would be difficult to maintain.

iv. Dosage Form Index

It is the ratio of $C_{SS,max}$ to $C_{SS,}$min. Since the goal of controlled release formulation is to improve therapy by reducing the dosage form index while maintaining the plasma level within the therapeutic window, ideally its value should be closed one.

C. Pharmacodynamic Characteristics of the Drug[33, 34]

i. Therapeutic Range

Drugs for SDDS should have a wide therapeutic range.

ii. Plasma Drug Concentration – Response Relationship

Drug whose pharmacological activity is independent of its concentration are poor candidates for SDDS.

2. LITERATURE REVIEW

- **Ruiz, J.M.** developed the procedure for the micro-encapsulation of peptide, a study of the phase-separation of poly(D,L-Lacto acid-Co-glycolic acid) co-polymers 50/50 by silicon oil.[12]
- **Chowdary, K.P.R.** demonstrated microencapsulation by calcium alginate. The evaluation of release kinetics suggested that all the microcapsules were found to be discrete spherical and free flowing.[13]

- **Pitchaimani, R.** shown comparative evaluation of Norfloxacin containing microcapsules by coacervation phase separation method. The release kinetics from the cellulose acetate micro capsules was found to be slower than that obtained from gelatin microcapsules.[14]
- **Chowdary, K.P.R.** prepared the microcapsules of Nifedipine by solvent evaporation method. The release depended on proportion of MCC in Solvent deposited systems used as core, coat, core ratio and size of microcapsules.[15]
- **Gohel, M.C.** prepared Diclofenac sodium microspheres by emulsion solvent evaporation technique. The stirring speed, polymer to drug ratio, concentration of ethyl cellulose solution and type of solvent were found to influence the in vitro drug release from the microspheres.[16]
- **Doshi, C.C.** prepared the levonorgestrel loaded biodegradable microspheres by emulsion solvent evaporation technique. The release kinetic of LNG from the microspheres was observed to be dependent on the ethanol content of the dissolution media.[17]
- **Hoffart, V.** demonstrated micro-encapsulation of low molecular weight Heparin. They shown encapsulation efficiency and release rate strongly depend on distribution of drug.[18]
- **Youan Celestin Bi-Botti**. developed micro-encapsulation of superoxide dismutase by reverse micelle solvent evaporation. This formulation allowed the in vitro release of superoxide dismutase for at least 72 hrs.[19]
- **Chowdary, K.P.R.** prepared the mucoadhesive microcapsules of Indomethacin by emulsification-ionic gelation process. They showed drug release was diffusion controlled and followed first order kinetics.[20]
- **Hasan, N.Y.** demonstrated stability indicating methods for the determination of Aceclofenac. Applciation of the proposed methods could be applied as stability indicating methods for the determination of pure aceclofenac and in presence of diclofenac either in the bulk powder or in pharmaceutical formulation.[21]
- **Fulzele, S.V.** prepared and evaluated microcapsules using polymerized resin and developed the in vitro dissolution study confirmed the Higuchi-order release pattern.[22]
- **Acuna, J.A.** developed the polarographic behaviour of Aceclofenac in a methanol-water mixture. [23]

- **Assimopoulou, A.N.** prepared the alkanin containing microcapsules by solvent evaporation method and studied the high release rate and a great extent of particle size of alkanin microencapsulation.[24]
- **Murthy, T.E.G.K.** developed the formulation and evaluation of Ethyl cellulose-coated diclofenac sodium microcapsules and studied diclofenac release from the microcapsule was followed first order kinetics and influenced by the size of the microcapsules. Among the solvent employed chloroform was found to be more suitable for slow release of diclofenac from ethyl cellulose microcapsules.[25]
- **Sahoo, S. K.** prepared stavudine by solvent evaporation method and studied that the best fit release kinetics was achieved with Higuchi plot followed by Zero order and first order. The release of stavudine was influenced by the drug to polymer ratio and particle size was found to be diffusion controlled.[26]
- **Gowda, K.V.** demonstrated the evaluation of bioequivalence of two formulations containing 100 mg of aceclofenac and suggested that 90% confidence interval for the ratio of the logarithmic transformed AUC_{o-t}, $AUC_{o-\infty}$ and C_{max} were within the bioequivalence limit 0.80 – 1.25.[27]
- **Bolourtchian, N**. studied on microencapsulation of Ibuprofen and discussed its characterization.[28]
- **Yang, C**. demonstrated the microencapsulation of Aspirin with Ethylcellulose by solvent evaporation method.[29]
- **Sajeev, C.** prepared oral controlled release formulation of Diclofenac sodium by microencapsulation using Ethylcellulose.[30]
- **Rolland *et al*** studied the characterization of microspheres using different drugs.[31]
- **Dorle, A. K.** studied microencapsulation using Eudragit polymer.[32]
- **Patel, J. K.** reported formulation and evaluation of mucoadhesive Glipizide microspheres.[39]
- **Shanmugum, S.** reported analysis method for Aceclofenac.[40]
- **Mahaparale, P. R**. reported analytical methods for estimation of Aceclofenac with Paracetamol in tablet dosage form.[41]
- **Geetharao, C. G.** reported studies on microspheres as targeting and controlled release.[42]

3. DRUG & POLYMER PROFILE

3.1. DRUG PROFILE[6, 7]

1. Aceclofenac:

A. Physio-chemical Properties of the drug –

1. Description

a. Nomenclature

i. Chemical name

A phenyl acetic acid derivative

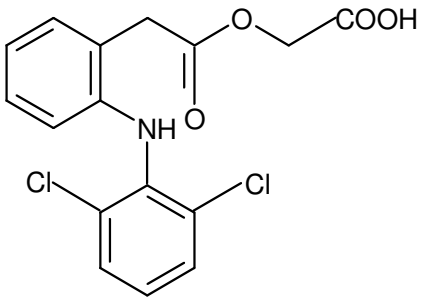
(2-{(2, 6-dichlorophenyl) amino} Phenyl acetoxy acetic acid)

ii. Generic name

Aceclofenac

b. Molecular weight and Formula

Molecular weight = 354.19



2. Appearance, **Colour**

A white or almost white crystalline powder

3. Solubility

Solvent	**Solubility**
Alcohol	Soluble
Acetone	Freely soluble
Water	Practically insoluble
Dichloromethane	Sparingly soluble

2 Pharmacokinetic Properties[38]

i. Oral absorption - Rapidly absorbed

ii. Bioavailability - Almost 100%

iii. Distribution - Highly protein – bound (>99.7%)

iv. Elimination -The mean plasma elimination half life is 4-4.3 hours. Clearance is estimated to 5 litres per hour. Approx. two-third of the administered dose is excreted via the urine, mainly as conjugated hydroxymetabolites. Only 1% of an oral single dose is excreted unchanged. Aceclofenac is probably metabolized via CYP2C9 to the main metabolite 4-hydroxy-Aceclofenac.

v. Dose - Maximum recommended dose is 200 mg daily takes as two separate 100 mg doses, one tablet in the morning and one in the evening. Aceclofenac can be taken before or after food.

vi. Therapeutic Indication - Symptomatic treatment of pain and inflammation of post traumatic pain, cervical pain and low back pain.

3 Pharmacodynamic Properties[35]

a. Category

A novel non-steroidal anti-inflammatory drug.

b. Mechanism of Action

Aceclofenac is a novel NSAID known to exhibit multifactor mechanism of action. Aceclofenac was developed in order to provide a highly effective pain relieving therapy with a reduced side-effect profile, especially GI events that are frequently experienced with NSAID therapy.

a. Aceclofenac directly blocks PGE_2 secretion at the site of inflammation by inhibiting IL-Beta and TNF in the inflammatory cells (Intracellular action).
b. Aceclofenac stimulates the synthesis of the extracellular matrix of the Human Articular cartilages.
c. Aceclofenac inhibits Neutrophil Adhesion and Accumulation at the inflammatory site in the early phase and thus blocks the pro-inflammatory actions of Neutrophils.
d. Aceclofenac is also an NSAID with a greater COX-2 specificity when compared to Diclofenac sodium.

c. Adverse effects

a. Mild to moderate liver cirrhosis

b. Renal impairment (mild to moderate)

3.2. POLYMER PROFILE[8]

1. Ethyl Cellulose

i. Chemical name	- Cellulose ethyl ether
ii. Description	- It is a white, tasteless, free flowing powder
iii. Functional category	- Coating agent, tablet binder, tablet filler
iv. Solubility	- Practically insoluble in water, freely soluble in Chloroform, soluble in dichloromethane
v. Applications	- It is a good polymer which is more suitable in sustained Release formulation of most of the drug - It is water impermeable in nature - For microencapsulation it is used in concentration of 10 to 20% (w/v) - Ethyl cellulose coating is used to modify the release of a drug, to improve the stability of a formulation.

2. Poly-vinyl pyrolidone (PVP)

i. Functional category	- Coating agent, tablet binder, tablet filler
ii. Solubility	- Soluble in acetone
iii. Application	- PVP is used as a poreformer in the microcapsules due to its water permeability nature

4. OBJECTIVE

The goal of therapy for any disease is to provide and enhance the patient well-beingness with least or no local systemic side effects after the administration of the drug. Unfortunately many of the administered conventional dosage forms will causes local or systemic side effects and unavoidable fluctuations in blood level of the drug. As a result it is difficult to achieve such a goal of therapy and this leads to poor patient compliance. To overcome such a problem and to improve patient compliance controlled release drug delivery systems was developed.

The main objective of the present studies is an effort to prolong the action of the drug Aceclofenac by formulating in microcapsules drug delivery system using different polymers and to explore suitability of the polymer for the same.

5. PLAN OF WORK

1. Preformulation studies.

i) Physical appearance.

ii) Characterization of drug.

- UV Spectrum
- IR Spectrum

iii) Scanning and preparation of standard curve by Spectrophotometeric method.

2. Preparation of Aceclofenac micro-capsules using different polymers such as –

i. Ethyl Cellulose

ii. Poly Vinyl Pyrrolidone

3. Evaluation of Aceclofenac microcapsules, such as

i. Determination of drug encapsulation efficiency
ii. In vitro dissolution studies
iii. Particle size and shape determination
iv. Drug – polymer compatibility study
    - FTIR Study

6. EXPERIMENTAL WORK

6.1. PREFORMULATION STUDIES:

6.1.1. Physical appearance:

Aceclofenac is a white or almost white crystalline powder.

6.1.2. Characterization of drug:

Ultraviolet spectroscopy test:

50mg of the drug was dissolved in methanol and diluted to 100ml with the same solvent. 2ml of the solution was diluted to 50ml with methanol. Then it was examined between 220nm and 370nm wavelength. The solution showed an absorption maximum at 275nm. The specific absorbance at the maximum is 320-350nm.

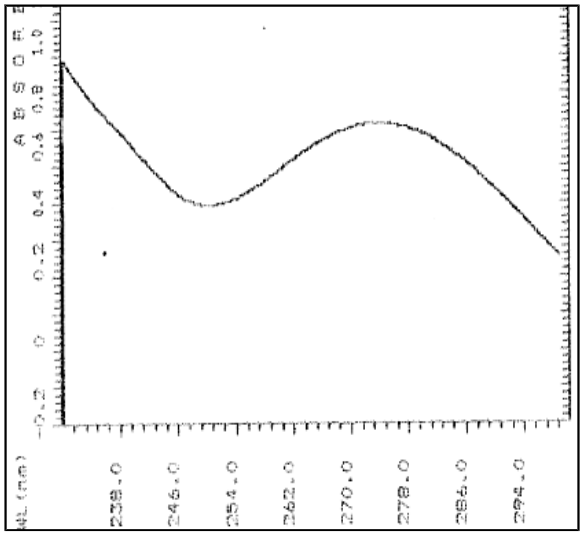
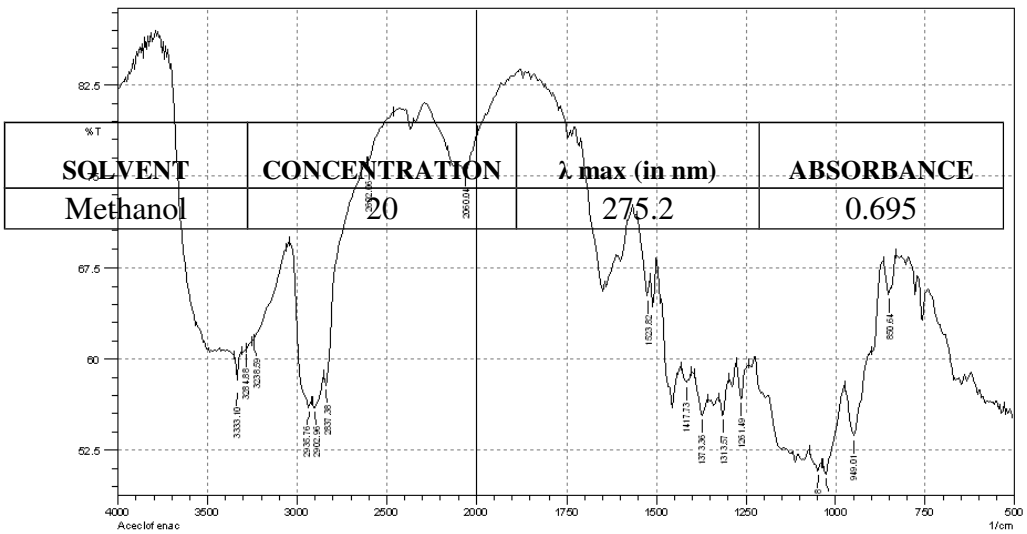


Fig. 2: UV SPECTRUM OF ACECLOFENAC IN METHANOL

Infrared spectroscopy test:

The infrared spectrum of potassium bromide dispersion of Aceclofenac is in accordance with the reference spectrum.



SOLVENT	CONCENTRATION	λ max (in nm)	ABSORBANCE
Methanol	20	275.2	0.695

Fig. 3: IR SPECTRA OF ACECLOFENAC WITH MAJOR PEAKS AT 3333.10, 2935.76, 1720.56, 1523.36, 1313.57, 850.64

6.1.3. Scanning of the drug:

Aceclofenac was scanned in these solvents –

a. Methanol
b. Phosphate buffer (pH 7.2)

Scanning of Drug in Methanol

Aceclofenac was scanned in methanol as per European – Pharmacopoeial method. 10 mg of drug was dissolved in 100 ml of methanol. This gave the solution concentration of 100 mcg/ml used as a stock solution. Then it was further diluted to 30mcg/ml. The prepared solution was scanned in the UV region from 220-370 nm. A characteristic peak was observed at 275 nm.

Scanning of the Drug in phosphate buffer pH 7.2

10 mg of drug was dissolved in 100 ml of phosphate buffer pH 7.2. This gave the solution concentration of 100 mcg/ml used as a stock solution. Then it was further diluted to 30mcg / ml. The prepared solution was scanned in the UV region from 220-370 nm. A characteristic peak was observed at 275.4 nm.

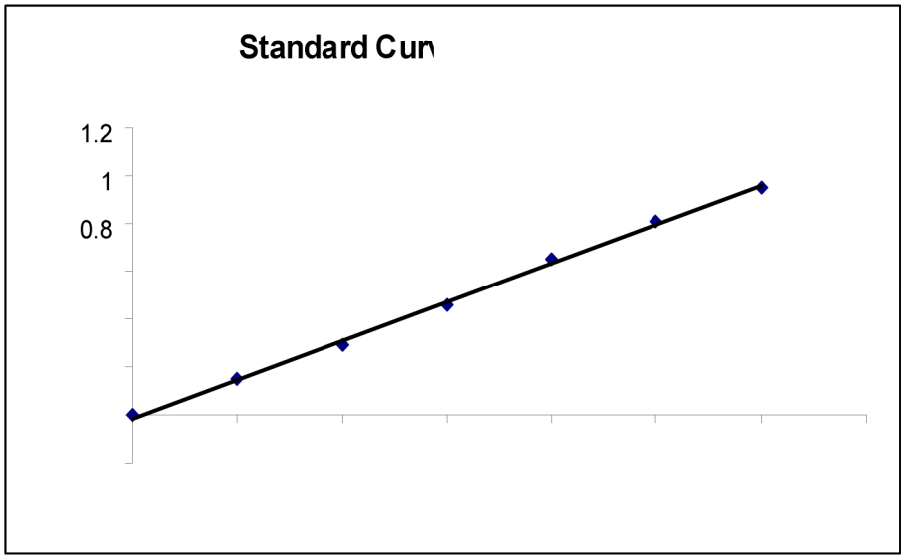
6.1.4. Standard plot of drug with solvent methanol[36]

Accurately weighed 10 mg of drug was dissolved in 100ml of methanol. Then diluting it 2.5, 5, 7.5, 10, 12.5, 15 to 50ml respectively. This gave the concentration of 5, 10, 15, 20, 25; 30mcg/ml and the absorbance were taken against the λmax at 275nm.

Concentration (mcg/ml)	Average Absorbance
5	0.147
10	
0.293	
15	0.458
20	0.653
25	0.807

(Each absorbance were taken in triplicate)

By regression analysis, Correlation coefficient $R^2 = 0.9983$



Standard Plot of Drug with phosphate buffer (pH 7.2)

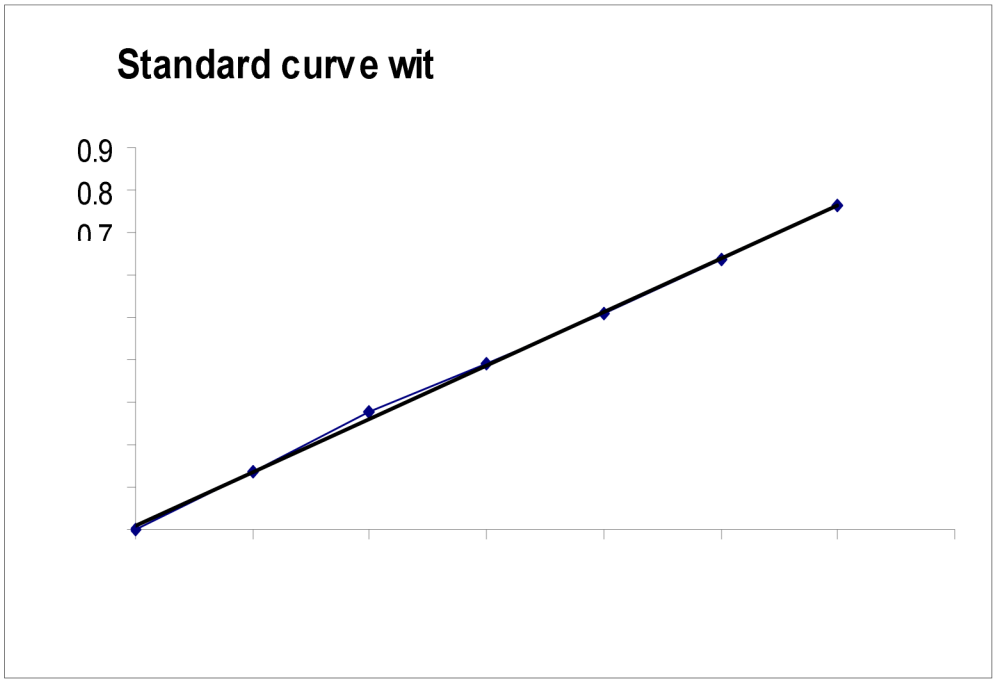
Accurately weighed 10mg of drug was dissolved in 100ml phosphate buffer. Then diluting it 2.5, 5, 7.5, 10, 12.5, 15 ml to 50ml respectively. This gave the concentration of 5, 10, 15, 20, 25, 30 mcg/ml and the absorbance were taken against the λ_{max} 275.4 nm.

Concentration (mcg/ml)	Average Absorbance
5	0.136
10	0.275
15	0.392
20	0.508
25	0.635

30	0.764

(Each absorbance were taken in triplicate)

By regression analysis, Correlation coefficient $R^2 = 0.9992$



Instruments and equipments used:

- Shimadzu UV-Pharmaspec 1700: UV Visible spectrophotometer.
- Mettler Toledo, Semi Micro Analytical balance. Model- AB104-s
- Systronics,µ-pH Meter, Model-361
- Magnetic Stirrer, Indian Equipment Corporation, Mumbai.
- FTIR, Shimadzu-Prestige-21.
- Lab India dissolution apparatus.
- Leica-DMF Microscope.

6.2. PREPARATION OF ACECLOFENAC MICROCAPSULES[37]

1. Materials

a) Aceclofenac obtained as a gift sample from IPCA Laboratories Ltd., Mumbai.
b) Ethyl cellulose
c) Polyvinyl pyrrolidone
d) Methanol
e) Dichloromethane
f) Acetone
g) Light liquid paraffin
h) Cyclohexane
i) Span 80

2. Method (Solvent evaporation method)

(i) Procedure

Different amount of polymer was dissolved in a solvent (acetone) using magnetic stirrer, to form a homogeneous polymer solution. The drug was dispersed in the polymer solution. The resulting dispersion was then poured in to the mixture of light liquid paraffin, cyclohexane and Span 80, while stirring. A mechanical stirrer was used for stirring. Stirring (at 800 to 1000 rpm) was continued for 3 hrs., until the solvent evaporated completely. After evaporation of solvent, the microcapsules formed were filtered using Whatmann filter paper (No. 1 grade). The residue was washed with 4 - 5 times in 50 ml cyclohexane each. Micro capsules were dried in desiccators for 24 hrs.

(ii) Formulation

Table 1: Formulation of Microencapsulation of Aceclofenac

S.No.	Ratio Drug : Polymer	Type of Polymer	Drug (mg)	Amount of Polymer	Solvent Acetone(ml)	Polymer conc. in solvent (% w/v)	External phase
1	1:1	Ethyl cellulose	500	500	10	5	Liquid paraffin

2	1:2	-do-	500	1000	10	10	
3	1:3	-do-	500	1500	10	15	
4	1:2	PVP	500	1000	10	10	
5	1:3	-do-	500	1500	10	15	
6	1:4	-do-	500	2000	10	20	

S.No.	Ratio Drug : polymer	Solvent	Concentration of polymer in solvent (% w/v)	External phase	Emulsifier	Emulsifier concentration (%v/v)	Result	Micro encapsulation efficiency (% w/v) (± S.D)
1	1:6	Acetone	30	Liquid paraffin	Span 80	1.96	Failure	……..
2	1:4		20			1.96	Failure	……..
3	1:3		15			1.96	Encapsulated	80.40±0.9848
4	1:2		10			1.96	Encapsulated	94.45±0.901
5	1:1		5			1.96	Encapsulated	96.01±0.115
6	1:1		5			1.96	Failure	……..

6.3. TRIALS:-

Table2: DIFFERENT TRIALS FOR MICRO-ENCAPSULATION WITH ETHYL CELLULOSE

Above mentioned all the trials were done in triplicate batches

Table 3: DIFFERENT TRIALS FOR MICRO-ENCAPSULATION WITH POLYVINYL PYRROLIDONE (PVP)

S.No.	Ratio Drug : polymer	Solvent	Concentration of polymer in solvent (% w/v)	External phase	Emulsifier	Emulsifier concentration (%v/v)	Result	Micro encapsulation efficiency (% w/v) (± S.D)
1	1:1	Acetone	5	Liquid paraffin	Span 80	0.99	Failure	……..
2	1:2		10			0.99	Encapsulated	92.5±1.135
3	1:3		15			0.99	Encapsulated	60.1±1.153
4	1:4		20			0.99	Encapsulated	46.44±0.787
5	1:6		30			0.99	Failure	……...

6.4. EVALUATION OF ACECLOFENAC MICROCAPSULES

i. Determination of Encapsulation efficiency of microcapsules:

Accurately weighed microcapsules containing 5mg equivalent amount of Aceclofenac was dissolved in the 50ml methanol and shaken vigorously. Then undissolved particles are removed by filtering through Whatmann filter paper. Finally 5 ml of this solution is diluted to 50 ml with respective blank solution and then its UV absorbance is to be noted.

Then the encapsulation efficiency is calculated by using the given below equation

$$\text{Encapsulation efficiency} = \frac{\text{Actual drug content}}{\text{Theoretical drug content}} \times 100$$

ii. Dissolution Rate study:

The in-vitro release studies of microcapsules were carried out at 37±1°c temperature and 100 rpm using phosphate buffer pH 7.2 in USP dissolution test apparatus (type II). Accurately weight samples of microcapsules (containing approximately 50 mg of drug) are taken in the muslin cloth ant tied properly to the paddles of the dissolution test apparatus, USP. 900 ml of dissolution media were used for analysis. The microcapsules were added to dissolution medium and at present time intervals 5 ml aliquots were withdrawn and replaced by an equal volume of fresh dissolution medium. Then it was further diluted up to 10 ml by taking 2ml of sample. After suitable dilution the sample were analyzed spectrophotometrically at 275.4 nm.

iii. Particle size analysis:

The prepared microcapsules were examined by optical microscopy using eye-piece micrometer. The eye-piece is calibrated with the help of stage micrometer. The mean diameter and particle size distribution of each formulation were measured by determination of the martin's diameter of 100 randomly selected particles.

iv. Drug-Polymer Compatibility Study

Drug-polymer compatibility is a critical parameter or factor to evaluate the efficiency of a formulation. For a stable and effective formulation, the drug-polymer interaction should be least. Despite of all the methods used for evaluation of drug-polymer interaction studies; the following two methods have been employed.

FT-IR spectroscopy: In this method the spectra were recorded for pure drug and drug loaded microcapsules using the instrument **IR-Prestige-21, Shimadzu, Japan**, employing KBr disc method. The scanning range was 400-4000 cm^{-1} and the resolution was 1 cm^{-1}.

7. RESULTS AND DISCUSSIONS

7.1 Characterization of bulk drug:

Supplied drug Aceclofenac passed the test for identification and analysis.

7.2 Preparation of microcapsule:

Ethylcellulose polymer was able to microencapsulate the drug Aceclofenac when the solvent for polymeric solution was acetone and external phase is containing Span 80 as an emulsifier. Also Ethylcellulose was able to encapsulate the drug when the concentration of the polymer was (5-15) % w/v in solvent.

The PVP polymer was able to microcapsulate the drug when the external phase was containing liquid paraffin. However, the PVP was able to encapsulate the drug only above 10% w/v and unable to encapsulate below it i.e 10% w/v.

7.3 Morphological and Microscopic characterization of Microcapsules:

A. Morphological characterization:

The Ethylcellulose microcapsules were freely flowing, white colored particles whereas PVP microcapsule were slightly aggregated particles.

B. Microscopic characterization:

The prepared Ethylcellulose microcapsules with different drug to polymer ratio (1:1, 1:2, 1:3) were uniform and almost spherical in appearance, whereas, PVP microcapsules using drug to polymer ratio (1:2, 1:3) were spherical but 1:4 ratio was mostly irregular.

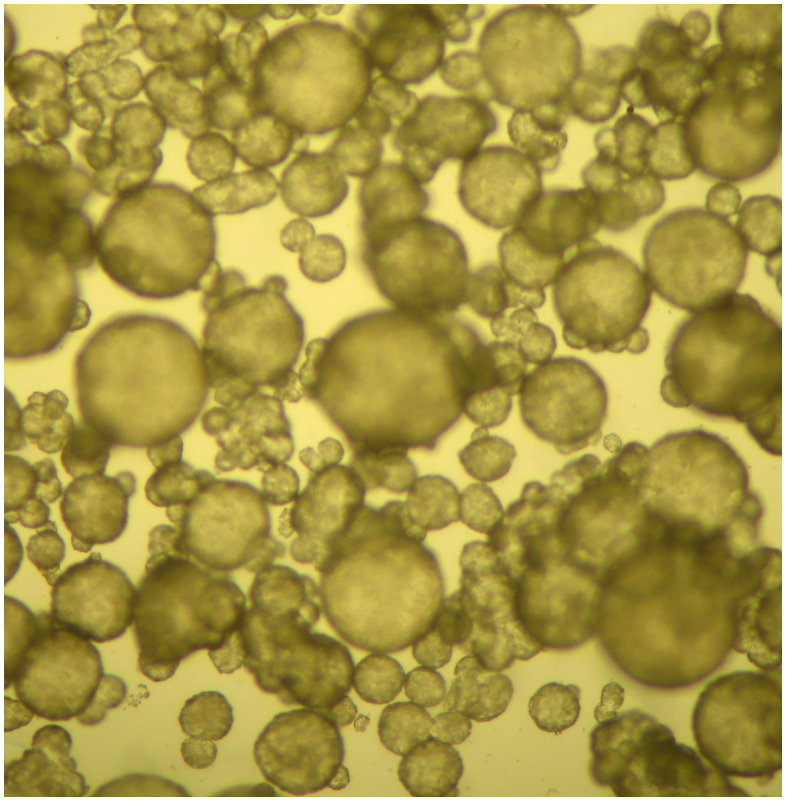


Fig. 4: Photograph of Ethylcellulose Microcapsules with drug:polymer ratio 1:1

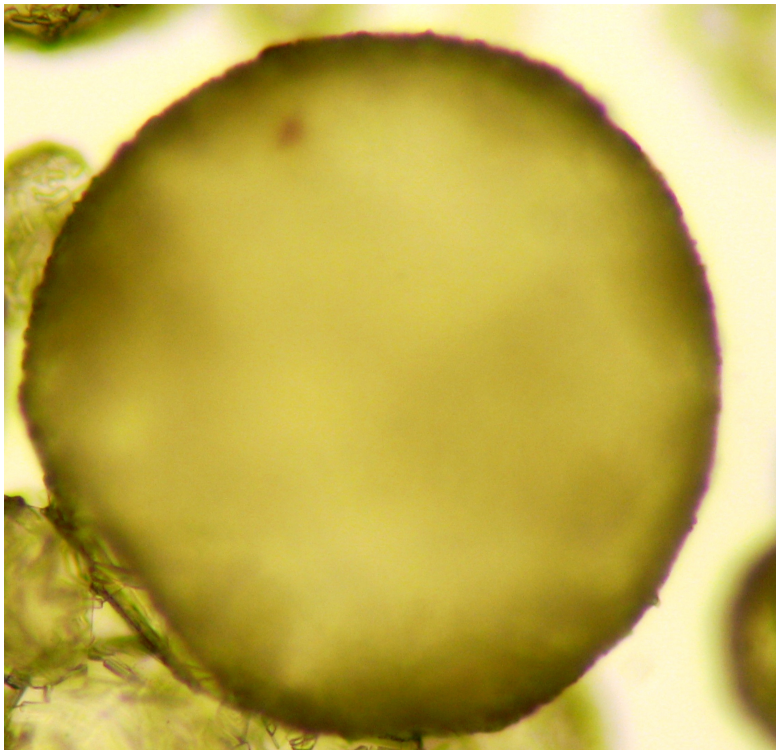


Fig. 5: Photograph of Ethylcellulose Microcapsules with drug:polymer ratio 1:1

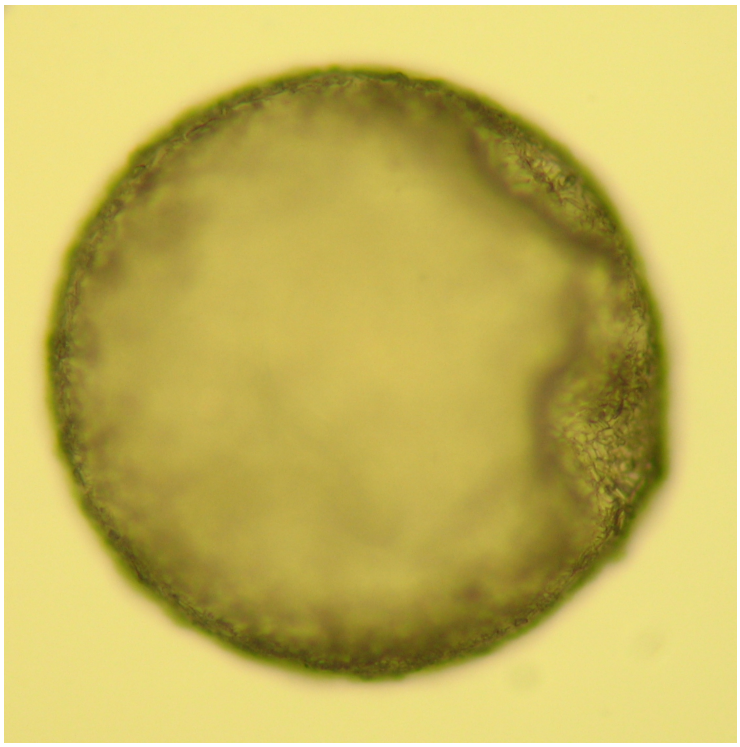


Fig. 6: Photograph of Ethylcellulose Microcapsules with drug:polymer ratio 1:2

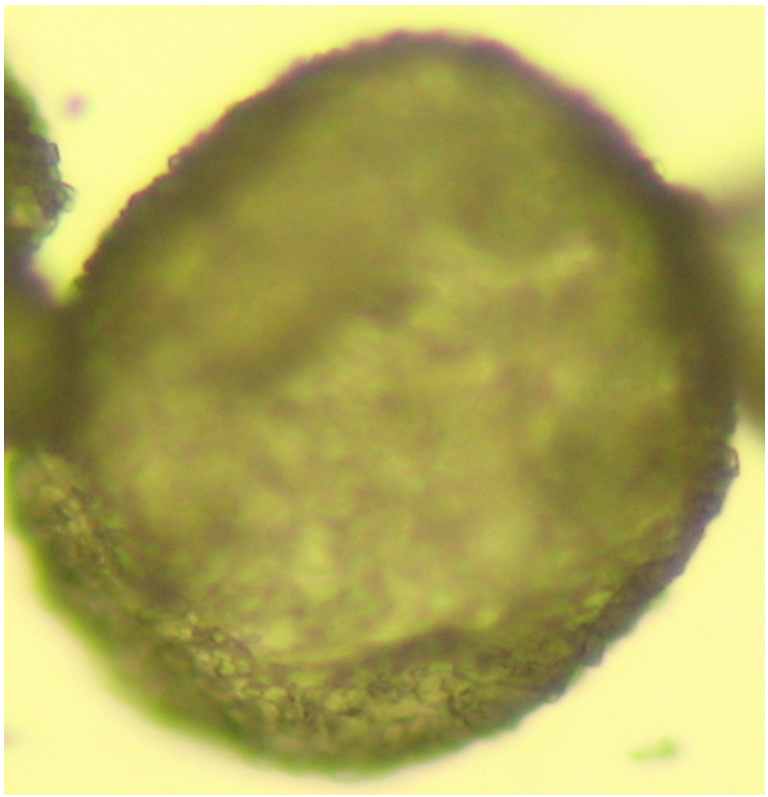


Fig. 7: Photograph of Ethylcellulose Microcapsules with drug:polymer ratio 1:3

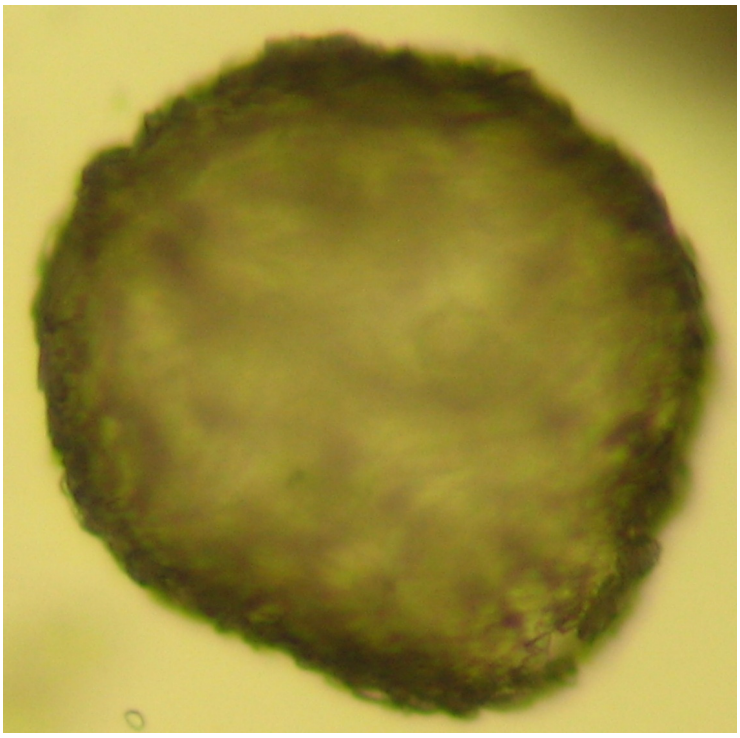


Fig. 8: Photograph of PVP Microcapsules with drug:polymer ratio 1:2

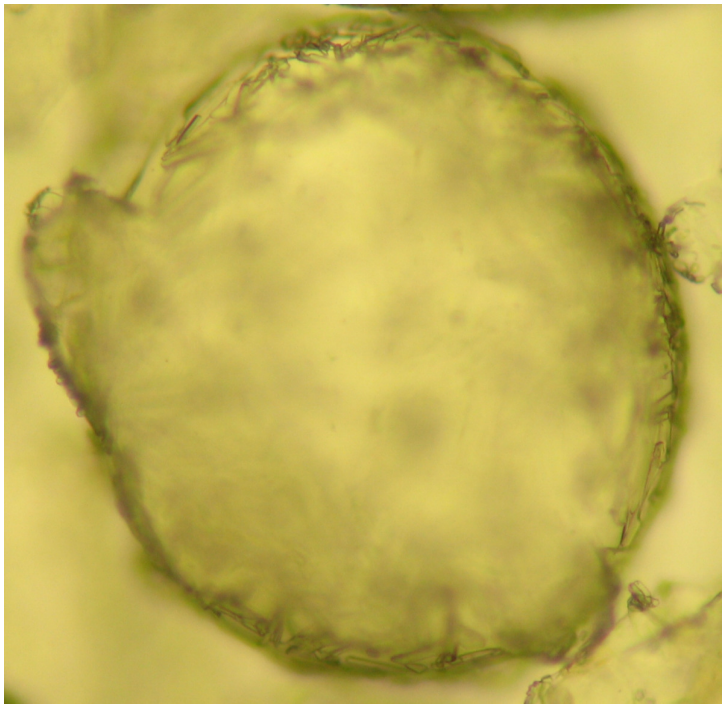


Fig. 9: Photograph of PVP Microcapsules with drug:polymer ratio 1:3

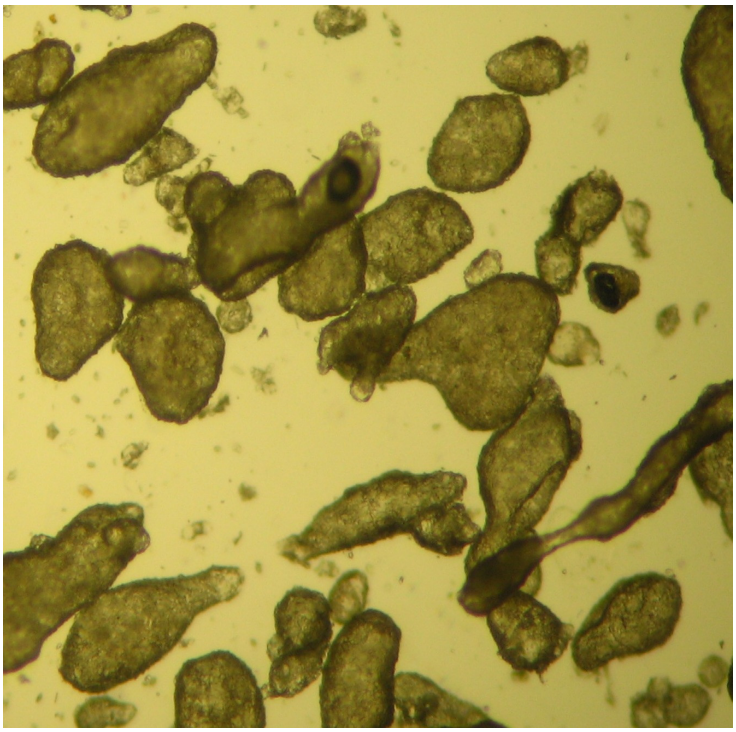


Fig. 10: Photograph of PVP Microcapsules with drug:polymer ratio 1:4

7.4 IN VITRO DISSOLUTION STUDIES

DISSOLUTION TEST—1

Polymer: Ethyl Cellulose
Ratio: 1:1
Polymer concentration: 5% (w/v)
Encapsulation efficiency: 96.0165%
Micro capsules weight:

1. 100mg
2. 100mg
3. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 4: Results of Dissolution Test-1

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.092	0.00653	5.87857	-	5.87857	6.97381± 2.67388	7.26362± 2.78500
	0.08	0.00557	5.02142	-	5.02142		
	0.15	0.01113	10.0214	-	10.0214		
2	0.342	0.02637	23.7357	0.03265	23.7683	22.6077± 1.03245	23.5473± 1.07536
	0.321	0.02470	22.2357	0.02789	22.2636		
	0.314	0.02415	21.7357	0.05567	21.7913		
3	0.452	0.03510	31.5928	0.16452	31.7573	31.7807± 0.80918	33.1015± 0.84281
	0.464	0.03605	32.45	0.15142	32.6014		
	0.441	0.03423	30.8071	0.17642	30.9835		
4	0.52	0.0405	36.45	0.34004	36.7900	36.9564± 0.22334	38.4922± 0.23262
	0.526	0.04097	36.8785	0.33170	37.2102		
	0.521	0.04057	36.5214	0.34757	36.8690		
6	0.669	0.05232	47.0928	0.54254	47.6354	48.1125± 0.95769	50.1117± 0.99749
	0.667	0.05216	46.95	0.53658	47.4865		
	0.691	0.05407	48.6642	0.55047	49.2147		
8	0.805	0.06311	56.8071	0.80416	57.6113	58.2336± 0.55470	60.6537± 0.57775
	0.82	0.06431	57.8785	0.79742	58.6759		
	0.816	0.06399	57.5928	0.82083	58.4136		
10	0.96	0.07542	67.8785	1.11976	68.9983	69.8622± 0.76378	72.7655± 0.79553
	0.976	0.07669	69.0214	1.11896	70.1404		
	0.98	0.07700	69.3071	1.14079	70.4479		
12	1.123	0.08835	79.5214	1.49686	81.0182	81.4821± 0.968412	84.8684± 1.008657
	1.145	0.090103	81.09286	1.502421	82.59528		
	1.12	0.088119	79.30714	1.525833	80.83298		

DISSOLUTION TEST— 2

Polymer: Ethyl Cellulose
Ratio: 1:2
Polymer concentration: 10% (w/v)
Encapsulation efficiency: 94.454%
Micro capsules weight:

4. 100mg
5. 100mg
6. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 5: Results of Dissolution Test-2

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.0968	0.006913	6.221429	-	6.221429	5.95238± 0.466004	6.3021± 0.493387
	0.0855	0.006016	5.414286	-	5.414286		
	0.0968	0.006913	6.221429	-	6.221429		
2	0.344	0.026532	23.87857	0.034563	23.91313	23.1259± 0.682799	24.4848± 0.722921
	0.327	0.025183	22.66429	0.030079	22.69437		
	0.328	0.025262	22.73571	0.034563	22.77028		
3	0.4	0.030976	27.87857	0.167222	28.04579	30.3494± 2.69979	32.1328± 2.858434
	0.474	0.036849	33.16429	0.155992	33.32028		
	0.423	0.032802	29.52143	0.160873	29.6823		
4	0.52	0.0405	36.45	0.322103	36.7721	36.9457± 0.239377	39.1167± 0.253444
	0.526	0.040976	36.87857	0.340238	37.21881		
	0.521	0.040579	36.52143	0.324881	36.84631		
6	0.769	0.060262	54.23571	0.524603	54.76032	53.8158± 0.896023	56.9781± 0.948674
	0.754	0.059071	53.16429	0.545119	53.7094		
	0.744	0.058278	52.45	0.527778	52.97778		
8	0.906	0.071135	64.02143	0.825913	64.84734	64.5166± 1.23724	68.3076± 1.309942
	0.882	0.06923	62.30714	0.840476	63.14762		
	0.916	0.071929	64.73571	0.819167	65.55488		
10	1.06	0.083357	75.02143	1.181587	76.20302	75.4180± 4.096422	79.8497± 4.337133
	1.1	0.086532	77.87857	1.186627	79.0652		
	0.987	0.077563	69.80714	1.17881	70.98595		
12	1.2123	0.095444	85.9	1.598373	87.49837	85.8852± 2.74811	90.9319± 2.909592
	1.145	0.090103	81.09286	1.619286	82.71214		
	1.212	0.095421	85.87857	1.566627	87.4452		

DISSOLUTION TEST— 3

Polymer: Ethyl Cellulose
Ratio: 1:3
Polymer concentration: 15% (w/v)
Encapsulation efficiency: 80.4086%
Micro capsules weight:

7. 100mg
8. 100mg
9. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 6: Results of Dissolution Test-3

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.079	0.0055	4.95		4.95	7.49761± 3.525659	9.32539± 4.385094
	0.094	0.00669	6.021429		6.021429		
	0.171	0.012802	11.52143		11.52143		
2	0.263	0.020103	18.09286	0.0275	18.12036	18.4678± 1.029679	22.9696± 1.280679
	0.284	0.02177	19.59286	0.033452	19.62631		
	0.256	0.019548	17.59286	0.064008	17.65687		
3	0.416	0.032246	29.02143	0.128016	29.14944	31.9749± 2.499506	39.7693± 3.108799
	0.468	0.036373	32.73571	0.142302	32.87802		
	0.482	0.037484	33.73571	0.161746	33.89746		
4	0.502	0.039071	35.16429	0.289246	35.45353	36.3422± 0.887108	45.2012± 1.103354
	0.514	0.040024	36.02143	0.324167	36.3456		
	0.526	0.040976	36.87857	0.349167	37.22774		
6	0.605	0.047246	42.52143	0.484603	43.00603	45.1614± 2.426671	56.1702± 3.01821
	0.628	0.049071	44.16429	0.524286	44.68857		
	0.671	0.052484	47.23571	0.554048	47.78976		
8	0.786	0.061611	55.45	0.720833	56.17083	54.7427± 3.289359	68.087± 4.091191
	0.798	0.062563	56.30714	0.769643	57.07679		
	0.712	0.055738	50.16429	0.816468	50.98075		
10	0.825	0.064706	58.23571	1.028889	59.2646	59.9950± 1.099414	74.6197± 1.367413
	0.827	0.064865	58.37857	1.08246	59.46103		
	0.852	0.066849	60.16429	1.095159	61.25944		
12	0.971	0.076294	68.66429	1.352421	70.01671	68.7271± 1.249375	85.4804± 1.55393
	0.951	0.074706	67.23571	1.406786	68.6425		
	0.935	0.073437	66.09286	1.429405	67.52226		

DISSOLUTION TEST— 4

Polymer: Poly vinyl pyrrolidone
Ratio: 1:2
Polymer concentration: 10% (w/v)
Encapsulation efficiency: 92.50%
Micro capsules weight:
10. 100mg
11. 100mg
12. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 7: Results of Dissolution Test-4

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.087	0.006135	5.521429	-	5.521429	6.85476± 2.753785	7.41047± 2.977033
	0.08	0.005579	5.021429	-	5.021429		
	0.15	0.011135	10.02143	-	10.02143		
2	0.292	0.022405	20.16429	0.030675	20.19496	18.0118± 1.894987	19.472± 2.048612
	0.248	0.018913	17.02143	0.027897	17.04933		
	0.244	0.018595	16.73571	0.055675	16.79139		
3	0.352	0.027167	24.45	0.142698	24.5927	23.5641± 1.111903	25.4744± 1.202044
	0.34	0.026214	23.59286	0.12246	23.71532		
	0.321	0.024706	22.23571	0.148651	22.38437		
4	0.4285	0.033238	29.91429	0.278532	30.19282	31.4466± 1.169494	33.9960± 1.264305
	0.4491	0.034873	31.38571	0.253532	31.63925		
	0.461	0.035817	32.23571	0.272183	32.5079		
6	0.589	0.045976	41.37857	0.444722	41.82329	42.2484± 0.630384	45.6734± 0.681489
	0.591	0.046135	41.52143	0.427897	41.94933		
	0.605	0.047246	42.52143	0.45127	42.9727		
8	0.805	0.063119	56.80714	0.674603	57.48175	55.5283± 1.781043	60.0299± 1.925431
	0.772	0.0605	54.45	0.658571	55.10857		
	0.756	0.05923	53.30714	0.6875	53.99464		
10	0.953	0.074865	67.37857	0.990198	68.36877	71.6902± 3.913883	77.5020± 4.231179
	0.986	0.077484	69.73571	0.961071	70.69679		
	1.06	0.083357	75.02143	0.983651	76.00508		
12	1.22	0.096056	86.45	1.364524	87.81452	87.4878± 0.286564	94.580± 0.309796
	1.214	0.095579	86.02143	1.348492	87.36992		
	1.212	0.095421	85.87857	1.400437	87.27901		

DISSOLUTION TEST— 5

Polymer: Poly vinyl pyrrolidone
Ratio: 1:3
Polymer concentration: 15% (w/v)
Encapsulation efficiency: 60.10%
Micro capsules weight:
13. 100mg
14. 100mg
15. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 8: Results of Dissolution Test-5

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.074	0.00510	4.59285	-	4.59285	5.11666± 0.57735	8.51358± 0.96064
	0.09	0.00637	5.73571	-	5.73571		
	0.08	0.00557	5.02142	-	5.02142		
2	0.173	0.01296	11.6642	0.02551	11.6898	13.1450± 1.67624	21.8720± 2.78908
	0.188	0.01415	12.7357	0.03186	12.7675		
	0.219	0.01661	14.95	0.02789	14.9779		
3	0.286	0.02192	19.7357	0.09031	19.8260	19.5989± 1.22599	32.6105± 2.03993
	0.298	0.02288	20.5928	0.10261	20.6954		
	0.264	0.02018	18.1642	0.11095	18.2752		
4	0.359	0.02772	24.95	0.19996	25.1499	25.9453± 1.24170	43.1702± 2.06606
	0.361	0.02788	25.0928	0.21702	25.3098		
	0.39	0.03018	27.1642	0.21186	27.3761		
6	0.487	0.03788	34.0928	0.33857	34.4314	33.1121± 1.16306	55.0950± 1.93522
	0.456	0.03542	31.8785	0.35642	32.235		
	0.462	0.03589	32.3071	0.36277	32.6692		
8	0.534	0.04161	37.45	0.52797	37.9779	37.508± 0.45765	62.4099± 0.76148
	0.527	0.04105	36.95	0.53353	37.4835		
	0.521	0.04057	36.5214	0.54226	37.0636		
10	0.566	0.04415	39.7357	0.73603	40.4717	39.9995± 0.59009	66.5549± 0.98184
	0.562	0.04383	39.45	0.73881	40.1888		
	0.55	0.04288	38.5928	0.74515	39.3380		
12	0.568	0.04431	39.8785	0.95678	40.8353	42.5985± 1.528633	70.8795± 2.543482
	0.606	0.04732	42.5928	0.95797	43.5508		
	0.604	0.04716	42.45	0.95956	43.40956		

DISSOLUTION TEST— 6

Polymer: Poly vinyl pyrrolidone
Ratio: 1:4
Polymer concentration: 20% (w/v)
Encapsulation efficiency: 46.44%
Micro capsules weight:
16. 100mg
17. 100mg
18. 100mg

Apparatus: Paddle with muslin cloth
R.P.M: 100
Volume: 900ml
Media: Phosphate buffer (pH 7.2)
Temperature: 37±1°C

Sampling volume = 5ml

Table 9: Results of Dissolution Test-6

TIME (hrs)	Absorbance (A1,A2,A3)	Conc^{n} (mg/ml)	Amount of drug release in 900 ml (mg)	Corr^{n} factor (mg)	Cumul. amount of drug release (mg)	Cumul. release (mg) Mean± S.D.	Cumul. % release Mean± S.D.
1	0.039	0.0023	2.0928	-	2.0928	2.045± 0.8581	4.404± 1.8478
	0.026	0.0013	1.1643	-	1.1642		
	0.050	0.0032	2.8785	-	2.8785		
2	0.081	0.0057	5.0928	0.0116	5.1044	5.604± 0.4346	12.067± 0.9359
	0.091	0.0065	5.8071	0.0064	5.8136		
	0.092	0.0065	5.8785	0.0159	5.8945		
3	0.098	0.0070	6.3071	0.0399	6.3470	6.492± 0.2442	13.980± 0.5259
	0.104	0.0075	6.7357	0.0387	6.7744		
	0.098	0.0070	6.3071	0.0486	6.3557		
4	0.122	0.0089	8.0214	0.0749	8.0963	8.433± 0.6381	18.158± 1.3741
	0.137	0.0101	9.0928	0.0761	9.1690		
	0.121	0.0088	7.9500	0.0837	8.0336		
6	0.179	0.0134	12.0928	0.1195	12.2123	11.765± 0.4267	25.334± 0.9189
	0.167	0.0125	11.2357	0.1266	11.3623		
	0.172	0.0129	11.5928	0.1278	11.7207		
8	0.221	0.0168	15.0928	0.1867	15.2795	15.615± 0.4089	33.625± 0.8805
	0.224	0.0170	15.3071	0.1890	15.4962		
	0.232	0.0176	15.8785	0.1922	16.0708		
10	0.279	0.0214	19.2357	0.2705	19.5062	19.629± 0.1138	42.269± 0.2451
	0.281	0.0215	19.3785	0.2741	19.6527		
	0.282	0.0216	19.4500	0.2804	19.7304		
12	0.327	0.0252	22.6642	0.3774	23.0417	23.784± 0.6448	51.216± 1.3885
	0.342	0.0264	23.7357	0.3817	24.1175		
	0.343	0.0265	23.8071	0.3885	24.1956		

Table 10 : DISSOLUTION PROFILE OF FORMULATIONS

TIME (IN HRS)	CUMULATIVE % OF DRUG RELEASED					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
1	7.26362	6.302	9.325	7.41	8.513	4.404
2	23.5473	24.484	22.969	19.472	21.872	12.067
3	33.1015	32.132	39.769	25.474	32.61	13.98
4	38.4922	39.116	45.201	33.996	43.17	18.158
6	50.1117	56.978	56.17	45.673	55.095	25.334
8	60.6537	68.3076	68.087	60.029	62.409	33.62
10	72.765	79.8497	74.619	77.502	66.554	42.269
12	84.8684	90.9319	85.48	94.58	70.879	51.216

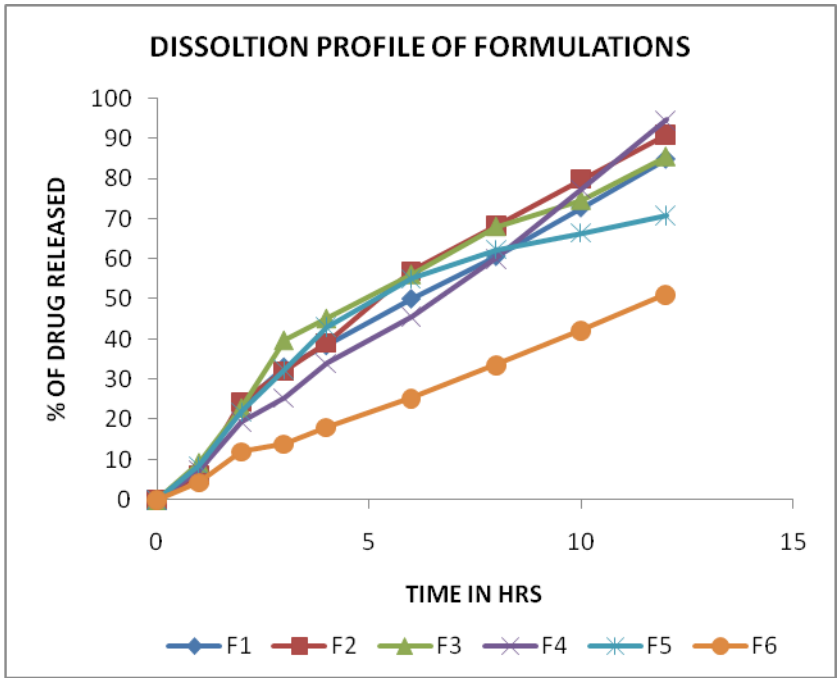


Figure 11: DISSOLUTION PROFILE OF FORMULATIONS

The percentage release of the drug from microcapsules formulated using different drug to polymer ratios was calculated using the following formula:

$$\text{Percentage release} = \frac{\text{Cumulative amount of drug release}}{\text{Encapsulation efficiency}} \times 100$$

Table 11: Results of Dissolution test for microcapsules prepared using different Drug-Polymer ratio.

S. No	Type of Polymer	Ratio (Drug: Polymer)	Time (hrs.) for 50% release	Time (hrs.) for 75% release	Time (hrs.) for 90% release
1	……	1:0 (Pure Drug)	…….	……	0.75±0.000
2	Ethylcellulose	1:1	6.58±2.567	9.88±0.560	11.85±1.073
3	-do-	1:2	6.05±1.167	9.09±2.638	10.90±1.567
4	-do-	1:3	6.21±1.727	9.32±1.519	11.18±2.878
5	PVP	1:2	6.39±1.046	9.59±0.206	11.51±1.303
6	-do-	1:3	7.01±0.532	10.51±0.516	12.61±0.642
7	-do-	1:4	6.86±1.061	10.29±1.782	12.35±1.361

Note: All the ratios were done in triplicate batches.

Calculations for above results:-

The above time taken for 50% or 75% or 90% release of drug is determined by $y = mx + c$,

Where, m = slope of the respective dissolution release rate curve.

C = intercept of the respective dissolution release rate curve

7.5 DRUG RELEASE KINETIC MODEL

The following are the tables for determining the kinetic model of release of the drug from microcapsules.

Table 12: Drug released kinetic model of Ethyl cellulose Microcapsules (1:1 Ratio)

S. No.	Time (hrs)	Square root of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of %Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	7.263628	92.73637	1.96725	4.52637
3	2	1.414214	23.54733	76.45267	1.883393	4.244217
4	3	1.732051	33.10155	66.89845	1.825416	4.059495
5	4	2	38.49228	61.50772	1.78893	3.947388
6	6	2.44949	50.11171	49.88829	1.697999	3.681286
7	8	2.828427	60.65375	39.34625	1.594903	3.401218
8	10	3.162278	72.76557	27.23443	1.435118	3.008658
9	12	3.464102	84.86843	15.13157	1.179884	2.473402

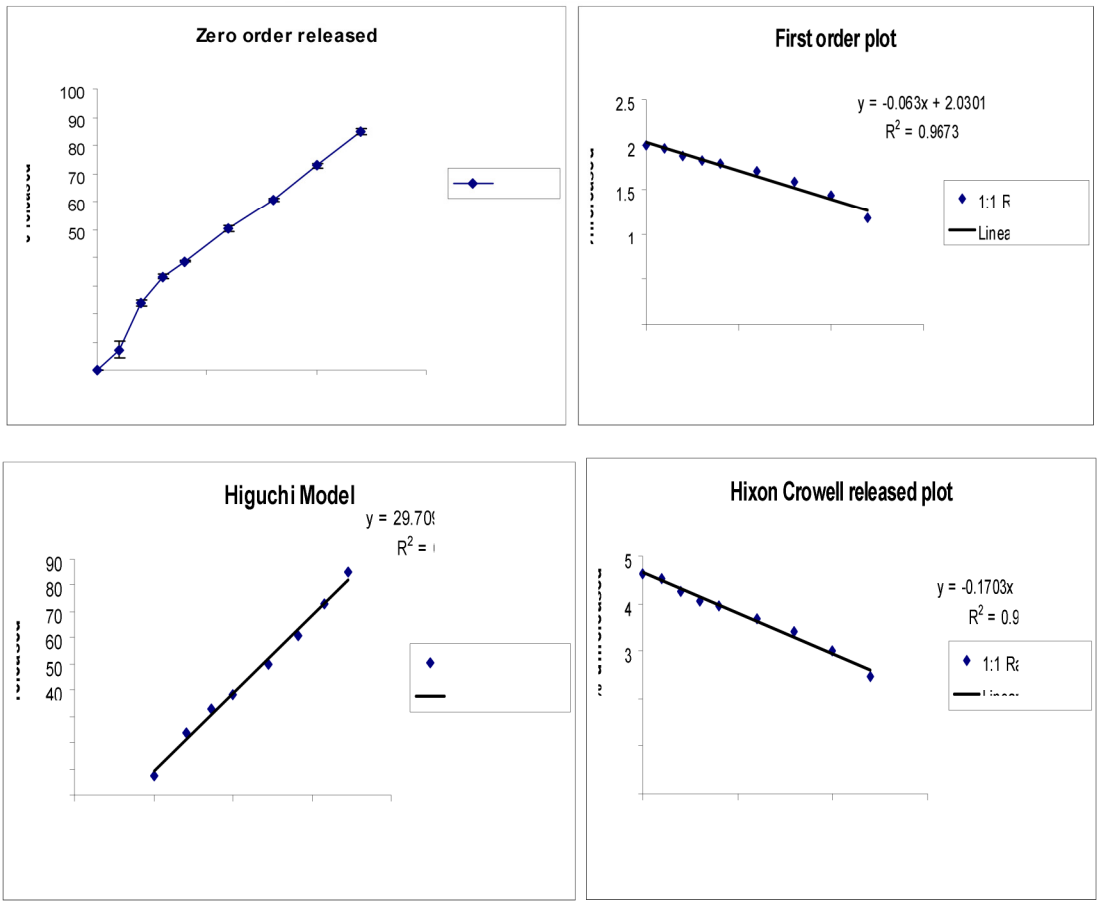


Figure 12: Drug released kinetic model of Ethyl cellulose Microcapsules (1:1 Ratio)

Table 13: Drug released kinetic model of Ethyl cellulose Microcapsules (1:2 Ratio)

S. No.	Time (hrs)	Square route of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of % Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	6.30215	93.69785	1.97173	4.541959
3	2	1.414214	24.48483	75.51517	1.878034	4.226797
4	3	1.732051	32.13283	67.86717	1.83166	4.078996
5	4	2	39.11672	60.88328	1.784498	3.933985
6	6	2.44949	56.97812	43.02188	1.633689	3.503992
7	8	2.828427	68.30769	31.69231	1.500954	3.164594
8	10	3.162278	79.84971	20.15029	1.304281	2.7212
9	12	3.464102	90.93196	9.068038	0.957513	2.085312

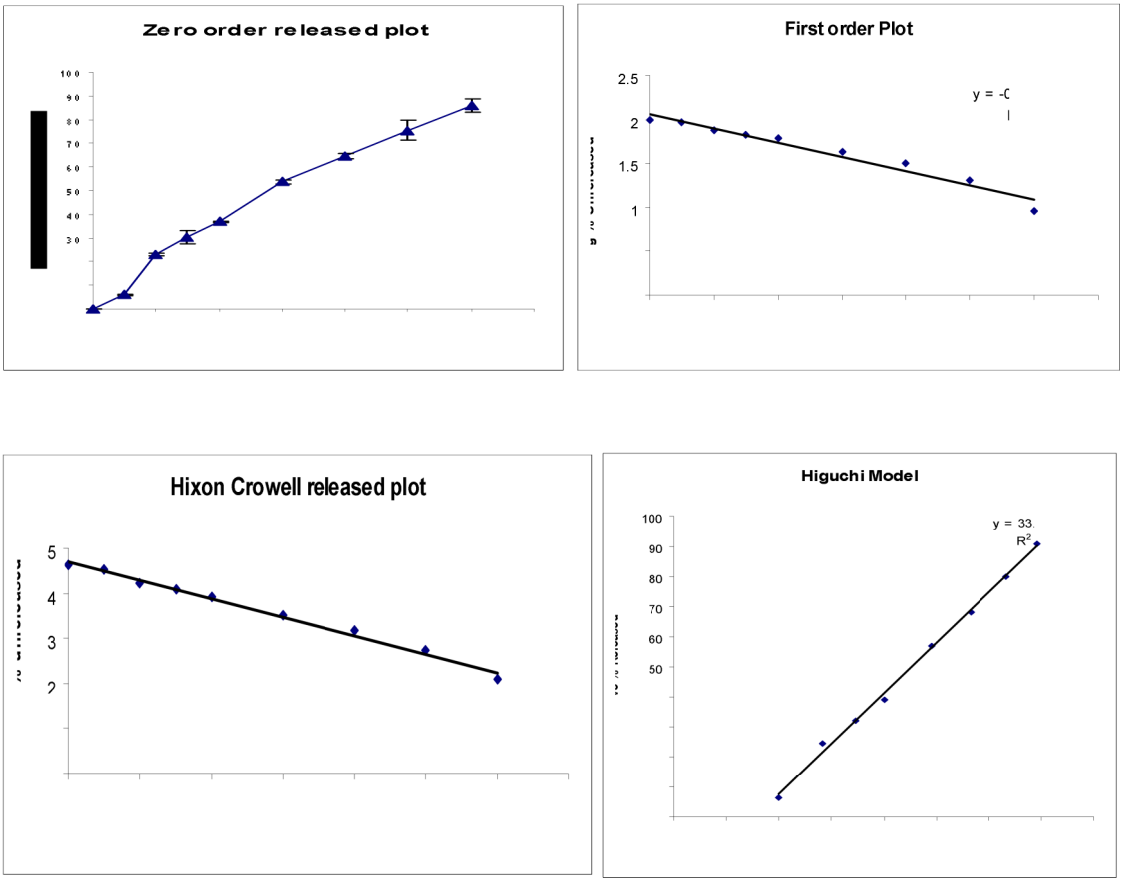


Figure 13: Drug released kinetic model of Ethyl cellulose Microcapsules (1:2 Ratio)

Table 14: Drug released kinetic model of Ethyl cellulose Microcapsules (1:3 Ratio)

S. No.	Time (hrs)	Square route of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of % Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	9.325397	90.6746	1.957486	4.492574
3	2	1.414214	22.96967	77.03033	1.886662	4.254879
4	3	1.732051	39.76937	60.23063	1.779817	3.919877
5	4	2	45.20129	54.79871	1.73877	3.798307
6	6	2.44949	56.17027	43.82973	1.641769	3.525789
7	8	2.828427	68.0872	31.9128	1.503965	3.171916
8	10	3.162278	74.61975	25.38025	1.404496	2.938768
9	12	3.464102	85.48047	14.51953	1.161952	2.439594

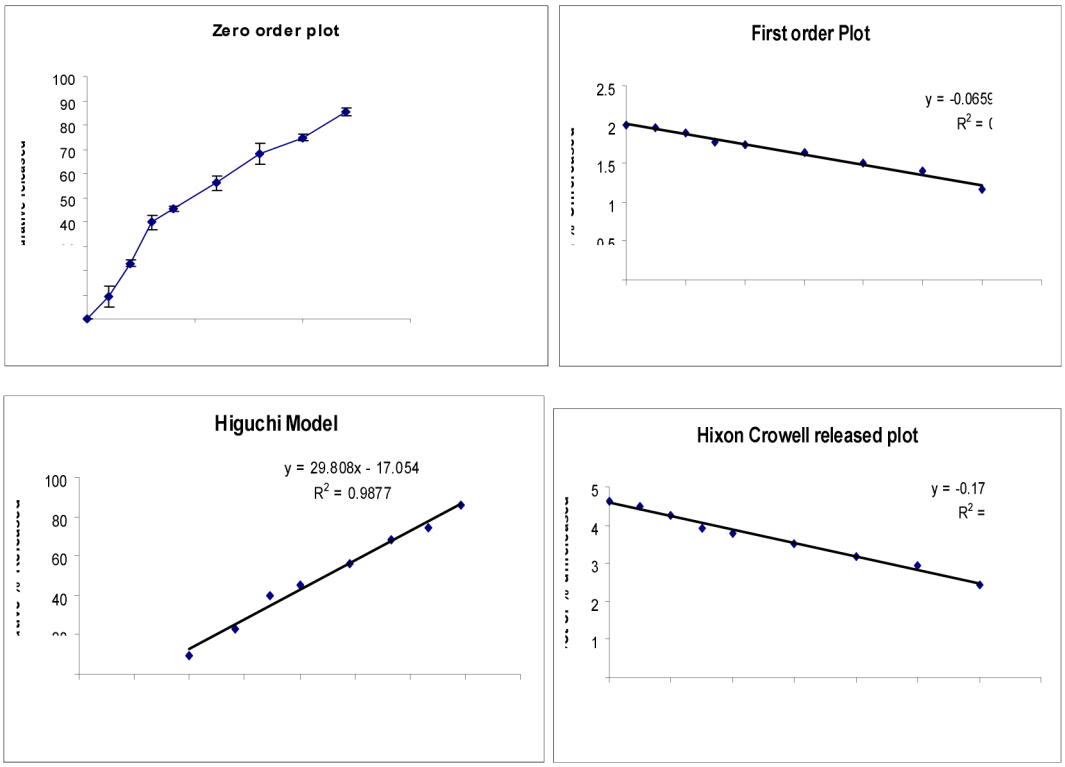


Figure 14: Drug released kinetic model of Ethyl cellulose Microcapsules (1:3 Ratio)

Table 15: Drug released kinetic model of Poly vinyl pyrrolidone Microcapsules (1:2Ratio)

S. No.	Time (hrs)	Square route of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of % Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	7.410473	92.58953	1.966562	4.523979
3	2	1.414214	19.4721	80.5279	1.905946	4.318326
4	3	1.732051	25.47446	74.52554	1.872305	4.208252
5	4	2	33.99601	66.00399	1.81957	4.041321
6	6	2.44949	45.67349	54.32651	1.735012	3.787366
7	8	2.828427	60.02997	39.97003	1.601735	3.419098
8	10	3.162278	77.50209	22.49791	1.352142	2.823021
9	12	3.464102	94.5804	5.419598	0.733967	1.756531

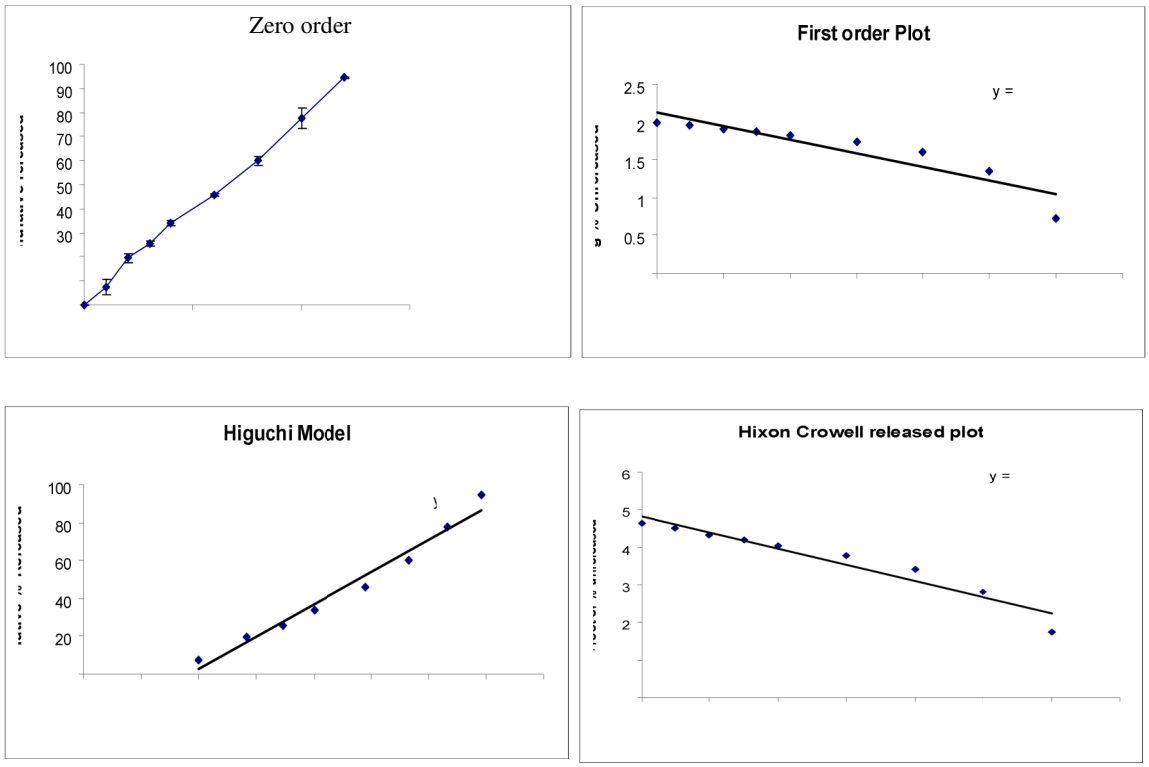


Figure 15: Drug released kinetic model of PVP Microcapsules (1:2 Ratio)

Table 16: Drug released kinetic model of PVP Microcapsules (1:3 Ratio)

S. No.	Time (hrs)	Square route of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of % Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	8.513588	91.48641	1.961357	4.505941
3	2	1.414214	21.87203	78.12797	1.892807	4.274994
4	3	1.732051	32.61051	67.38949	1.828592	4.069403
5	4	2	43.17027	56.82973	1.754576	3.844665
6	6	2.44949	55.09504	44.90496	1.652294	3.554388
7	8	2.828427	62.40998	37.59002	1.575073	3.349841
8	10	3.162278	66.55495	33.44505	1.524332	3.221889
9	12	3.464102	70.87951	29.12049	1.464199	3.076566

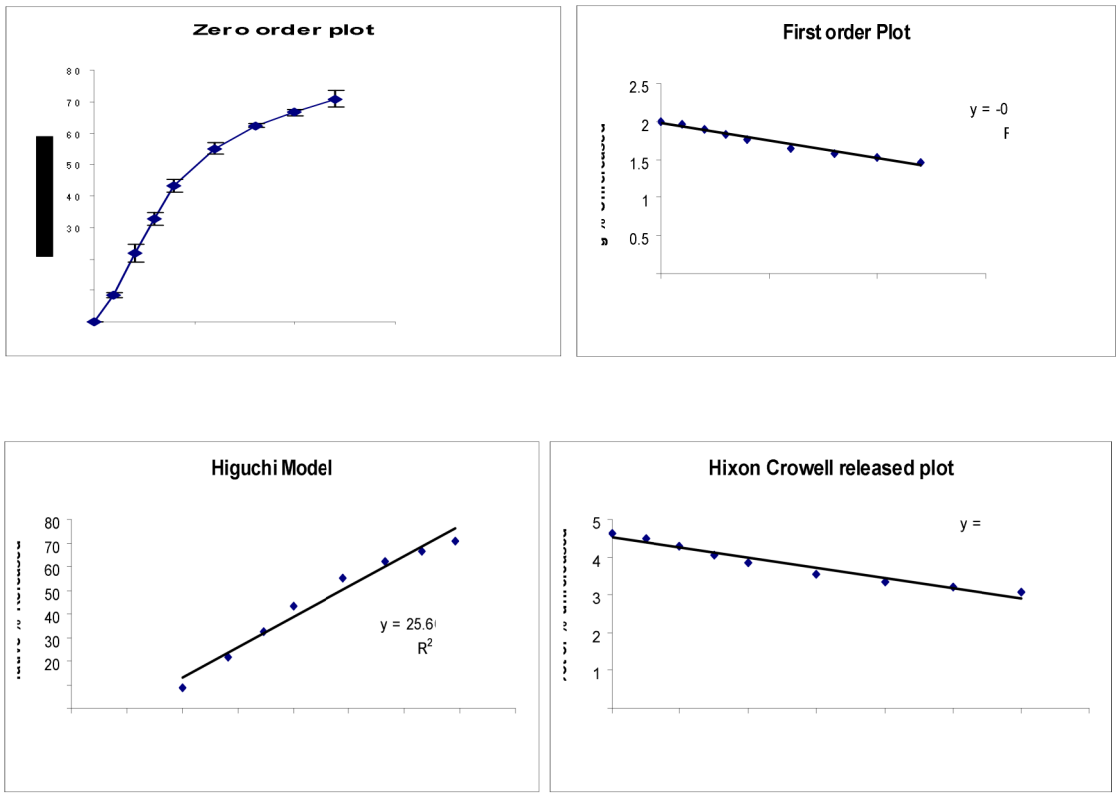


Figure 16: Drug released kinetic model of PVP Microcapsules (1:3 Ratio)

Table 17: Drug released kinetic model of PVP Microcapsules (1:4 Ratio)

S. No.	Time (hrs)	Square root of Time	% Drug Released	% Drug Unreleased	Log % Drug Unreleased	Cube root of %Drug Unreleased
1	0	0	0	100	2	4.641589
2	1	1	4.404044	95.59596	1.98044	4.572424
3	2	1.414214	12.06766	87.93234	1.944149	4.44682
4	3	1.732051	13.98026	86.01974	1.934598	4.414343
5	4	2	18.15898	81.84102	1.912971	4.341672
6	6	2.44949	25.33411	74.66589	1.873122	4.210892
7	8	2.828427	33.6252	66.3748	1.822003	4.048875
8	10	3.162278	42.2692	57.7308	1.761408	3.864879
9	12	3.464102	51.21654	48.78346	1.688273	3.653907

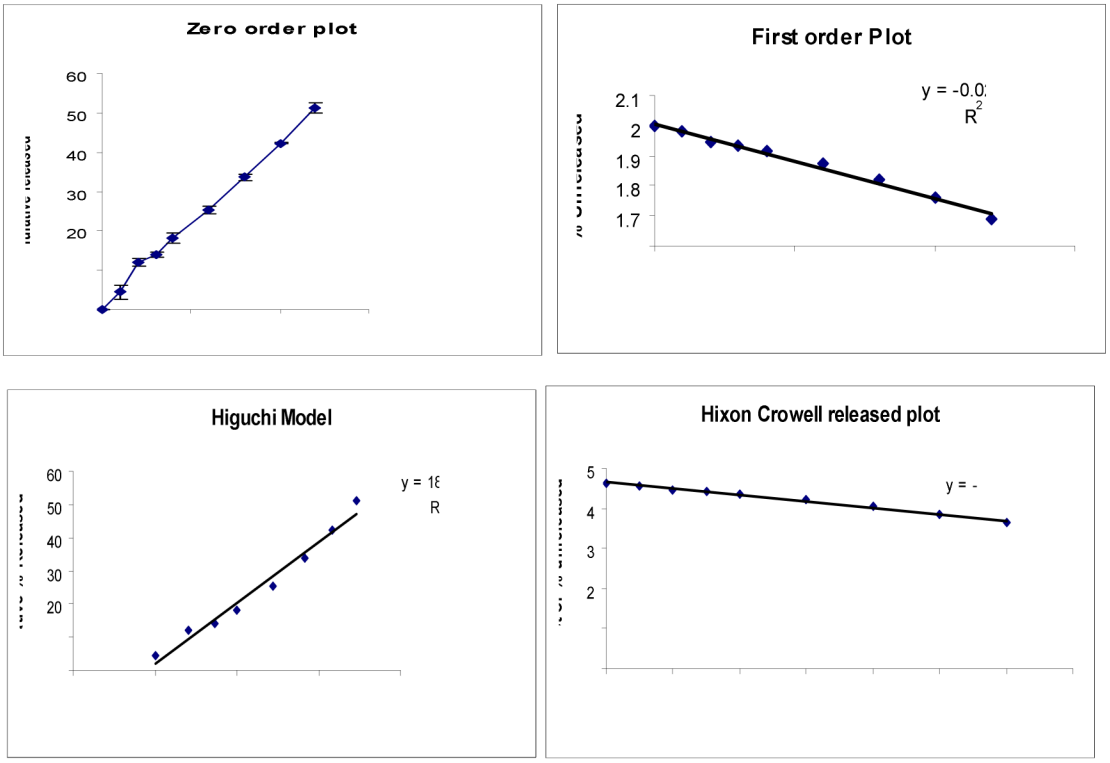


Figure 17: Drug released kinetic model of PVP Microcapsules (1:4 Ratio)

Drug Release Kinetic Model Report

Table 18: Drug release kinetic model report

S. No.	Type of polymer	Ratio Drug:Polymer	Correlation coefficient factor for drug release profiles(R_1)			
			Zero order	First order	Higuchi	Hixon Crowell
1.	Ethyl cellulose	1:1	0.9526	0.9673	0.9932	0.9876
2.	-do-	1:2	0.9641	0.9602	0.9973	0.9910
3.	-do-	1:3	0.9004	0.9857	0.9877	0.9884
4.	PVP	1:2	0.9957	0.8470	0.9728	0.9315
5.	-do-	1:3	0.8476	0.9734	0.9700	0.9556
6.	-do-	1:4	0.9935	0.9872	0.9728	0.9924

The above table shows that, the release kinetics of ethyl cellulose and poly vinyl pyrrolidone microcapsules have got a good correlation with the Higuchi model. The results indicated that, various drug : polymer ratios in microcapsule preparation did not change the release kinetics.

7.6 Particle Size Analysis:

Table 19: Particle size analysis of Ethyl cellulose micro capsules (1:1 Ratio)

S.No.	Size Range (micro meter)	Mean size range (micro meter)	No.of particles (Frequency)	nd	nd^2	nd^3
1.	0-50	25	1	25	625	15625
2.	50-100	75	8	600	45000	3375000
3.	100-150	125	12	1500	187500	23437500
4.	150-200	175	34	5950	1041250	1.82×10^8
5.	200-250	225	28	6300	1417500	3.19×10^8
6.	250-300	275	10	2750	756250	2.08×10^8
7.	300-350	325	7	2275	739375	2.4×10^8
			$\sum n=100$	$\sum nd=$ 19400	$\sum nd^2=$ 4187500	$\sum nd^3=$ 9.7625×10^8

S.No.	Equation for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (micro meter)	Comment
1	$\sum nd / \sum n$	Arithmetic	Length	Number	Length number	194	Refers to average particle Size
2	$\sqrt{\sum nd^2 / \sum n}$	-do-	Surface	-do-	Surface number	204.6338	Refers to average particle surface area
3	$\sqrt[3]{\sum nd^3 / \sum n}$	-do-	Volume	-do-	Volume number	213.7242	Refers to average particle surface area
4	$\sum nd^3 / \sum nd^2$	-do-	Length	Surface	Volume Surface	233.1343	Refers to average particle specific surface area (inversely related)

Table 20: Particle size analysis of Ethyl cellulose micro capsules (1:2 Ratio)

S.No.	Size Range (micro meter)	Mean size range (micro meter)	No.of particles (Frequency)	nd	nd^2	nd^3
1.	0-50	25	1	25	625	15625
2.	50-100	75	48	3600	270000	20250000
3.	100-150	125	18	2250	281250	35156250
4.	150-200	175	12	2100	367500	64312500
5.	200-250	225	8	1800	405000	91125000
6.	250-300	275	13	3575	983125	2.7×10^8
			$\sum n=100$	$\sum nd=$ 13350	$\sum nd^2=$ 2307500	$\sum nd^3=$ 4.8121875×10^8

S.No.	Equation for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (micro meter)	Comment
1	$\sum nd / \sum n$	Length	Number	Length number	133.50	Refers to average particle Size	
2	$\sqrt{\sum nd^2 / \sum n}$	Surface	-do-	Surface number	151.90		
3	$\sqrt[3]{\sum nd^3 / \sum n}$	Volume	-do-	Volume number	168.82	Refers to average particle surface area	
4	$\sum nd^3 / \sum nd^2$ Arithmetic	Length	Surface	Volume Surface	208.54	Refers to average	

	-do- -do- -do-					particle surface area Refers to average particle specific surface area (inversely related)	

Table 21: Particle size analysis of Ethyl cellulose micro capsules (1:3 Ratio)

S.No.	Size Range (micro meter)	Mean size range (micro meter)	No. of particles (Frequency)	nd	nd^2	nd^3
1	0-50	25	1	25	625	15625
2	50-100	75	3	225	16875	1265625
3	100-150	125	22	2750	343750	42968750
4	150-200	175	5	875	153125	26796875
5	200-250	225	5	1125	253125	56953125
6	250-300	275	14	3850	1058750	2.91×10^8
7	300-350	325	7	2275	739375	2.4×10^8
8	350-400	375	8	3000	1125000	4.22×10^8
9	400-450	425	7	2975	1264375	5.37×10^8
10	450-500	475	11	5225	2481875	1.18×10^8
11	500-550	525	9	4725	2480625	1.3×10^8
12	550-600	575	8	4600	2645000	1.52×10^9
			$\sum n=100$	$\sum nd=$ 31650	$\sum nd^2=$ 12562500	$\sum nd^3=$ 5620781250

S.No.	Eqn for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (μ meter)	Comment
1	$\sum nd / \sum n$	Arithmetic	Length	Number	Length number	316.5	Refers to average particle Size
2	$\sqrt{\sum nd^2 / \sum n}$	-do-	Surface	-do-	Surface number	354.4362	Refers to average particle surface area
3	$\sqrt[3]{\sum nd^3 / \sum n}$	-do-	Volume	-do-	Volume number	383.0589	Refers to average particle surface area
4	$\sum nd^3 / \sum nd^2$	-do-	Length	Surface	Volume Surface	447.4254	Refers to average particle specific surface area

S.No.	**Size Range (micro meter)**	**Mean size range (micro meter)**	**No. of particles (Frequency)**	**nd**	**nd^2**	**nd^3**
1	0-50	25	0	0	0	0
2	50-100	75	4	300	22500	1687500
3	100-150	125	9	1125	140625	17578125
4	150-200	175	14	2450	428750	75031250
5	200-250	225	21	4725	1063125	2.39×10^8
6	250-300	275	32	8800	2420000	6.66×10^8
7	300-350	325	7	2275	739375	2.4×10^8
8	350-400	375	8	3000	1125000	4.22×10^8
9	400-450	425	5	2125	903125	3.84×10^8
			$\sum n=100$	$\sum nd=$ 24800	$\sum nd^2=$ 6842500	$\sum nd^3=$ 20.45×10^8

Table 22: Particle size analysis of Poly vinyl pyrrolidone micro capsules (1:2 Ratio)

S.No.	Eqn for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (μM)	Comment
1	$\sum nd / \sum n$	Arithmetic	Length	Number	Length number	248	Refers to average particle Size
2	$\sqrt{\sum nd^2 / \sum n}$	-do-	Surface	-do-	Surface number	261.5817	Refers to average particle surface area
3	$\sqrt[3]{\sum nd^3 / \sum n}$	-do-	Volume	-do-	Volume number	273.4625	Refers to average particle surface area
4	$\sum nd^3 / \sum nd^2$	-do-	Length	Surface	Volume Surface	298.8674	Refers to average particle specific surface area

Table 23: Particle size analysis of Poly vinyl pyrrolidone micro capsules (1:3 Ratio)

S.No.	Size Range (micro meter)	Mean size range (micro meter)	No. of particles (Frequency)	nd	nd^2	nd^3
1	0-50	25	0	0	0	0
2	50-100	75	0	0	0	0
3	100-150	125	3	375	46875	5859375
4	150-200	175	22	3850	673750	1.18×10^8
5	200-250	225	26	5850	1316250	2.96×10^8
6	250-300	275	18	4950	1361250	3.74×10^8
7	300-350	325	8	2600	845000	2.75×10^8
8	350-400	375	4	1500	562500	2.11×10^8
9	400-450	425	11	4675	1986875	8.44×10^8
10	450-500	475	8	3800	1805000	8.57×10^8
			$\sum n=100$	$\sum nd=$ 27600	$\sum nd^2=$ 8597500	$\sum nd^3=$ 29.81625×10^8

S.No.	Eqn for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (μ meter)	Comment
			Length			Refers to average particle Size	
			Surface				
1	$\sum nd / \sum n$	Arithmetic	Volume	Length number	276.00	Refers to average particle surface area	
2	$\sqrt{\sum nd^2 / \sum n}$	-do-	Length Number	Surface number	293.21		
3	$\sqrt[3]{\sum nd^3 / \sum n}$	-do-	-do-	Volume number	310.08	Refers to average particle surface area	
4	$\sum nd^3 / \sum nd^2$	-do-	-do-	Volume Surface	346.80	Refers to average particle specific surface area	
			Surface				

Table 24: Particle size analysis of Poly vinyl pyrrolidone micro capsules (1:4 Ratio)

S.No.	Size Range (micro meter)	Mean size range (micro meter)	No. of particles (Frequency)	nd	nd^2	nd^3
1	0-50	25	0	0	0	0
2	50-100	75	0	0	0	0
3	100-150	125	12	1500	187500	23437500

4	150-200	175	39	6825	1194375	2.09×10^8
5	200-250	225	27	6075	1366875	3.08×10^8
6	250-300	275	3	825	226875	62390625
7	300-350	325	3	975	316875	1.03×10^8
8	350-400	375	6	2250	843750	3.16×10^8
9	400-450	425	6	2550	1083750	4.61×10^8
10	450-500	475	4	1900	902500	4.29×10^8
			$\sum n=100$	$\sum nd=$ 22900	$\sum nd^2=$ 6122500	$\sum nd^3=$ 19.110625×10^8

S.No.	Eqn for calculating diameter mean	Type of mean	Size parameter	Frequency	Mean diameter	Value (μ meter)	Comment
1	$\sum nd / \sum n$	Arithmetic	Length	Number	Length number	229.00	Refers to average particle Size
2	$\sqrt{\sum nd^2 / \sum n}$	-do-	Surface	-do-	Surface number	247.43	Refers to average particle surface area
3	$\sqrt[3]{\sum nd^3 / \sum n}$	-do-	Volume	-do-	Volume number	267.35	Refers to average particle surface area
4	$\sum nd^3 / \sum nd^2$	-do-	Length	Surface	Volume Surface	312.13	Refers to average particle specific surface area

Particle Size Analysis:

Histogram of Microcapsules:

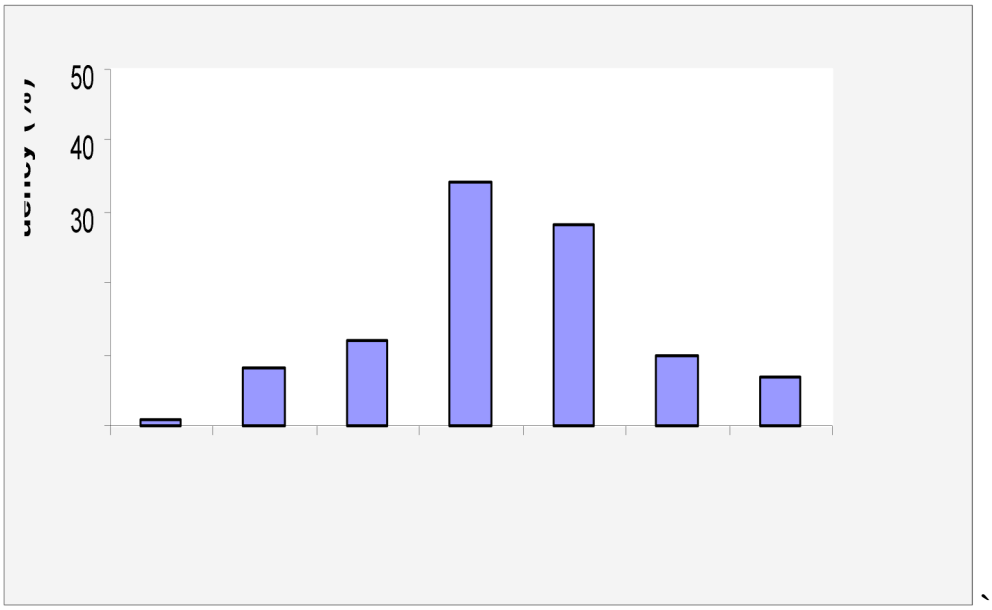


Figure 18: Histogram of particle size distribution for Ethylcellulose Microcapsule (1:1 ratio)

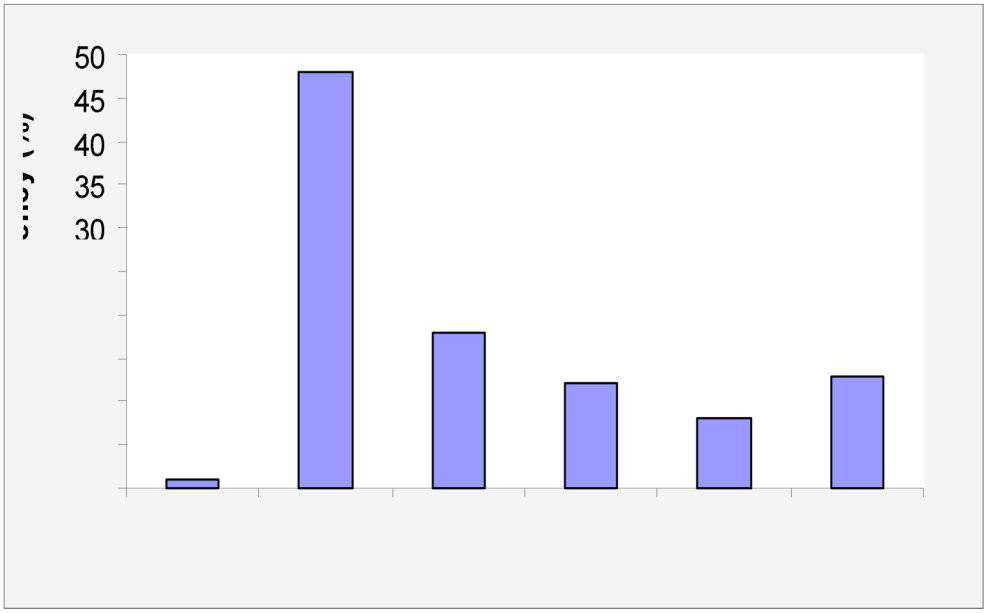


Figure 19: Histogram of particle size distribution for Ethylcellulose Microcapsule (1:2 ratios)

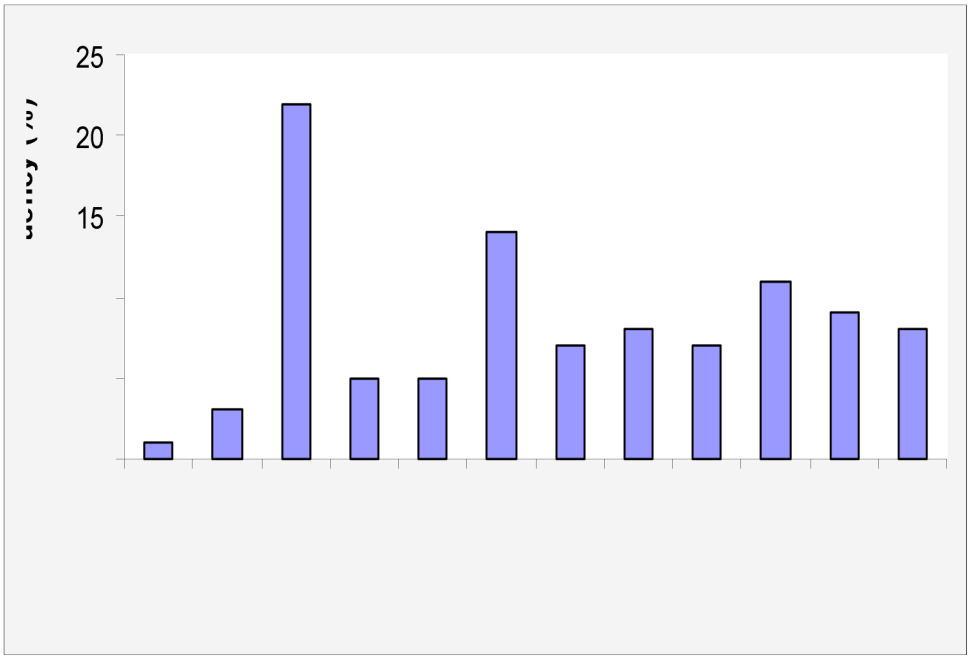


Figure 20: Histogram of particle size distribution for Ethylcellulose Microcapsule (1:3 ratios)

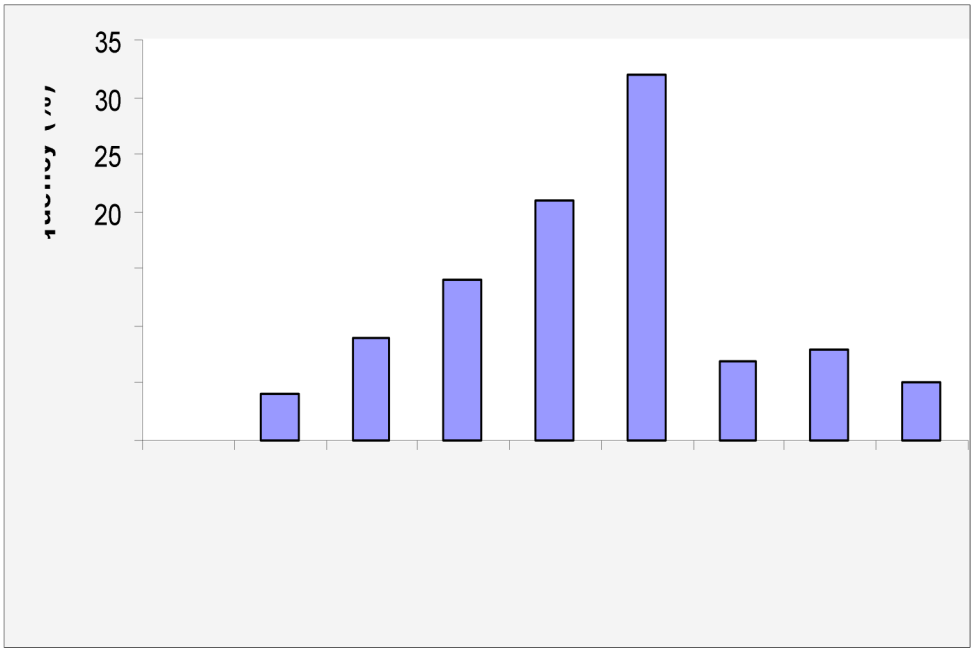


Figure 21: Histogram of particle size distribution for Polyvinylpyrrolidone Microcapsule (1:2 ratios)

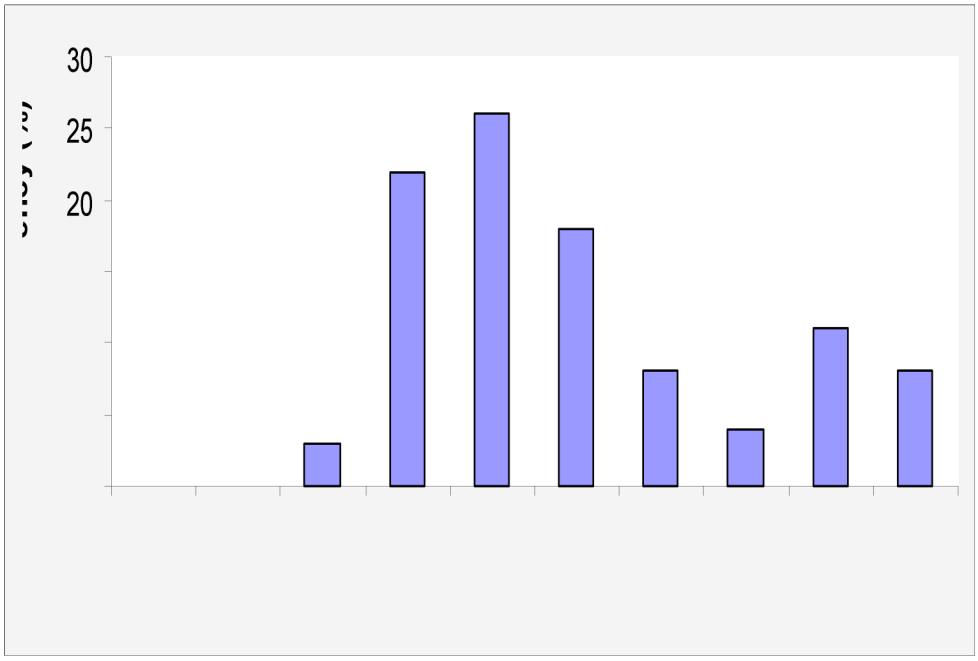


Figure 22: Histogram of particle size distribution for Polyvinylpyrrolidone Microcapsule (1:3 ratios)

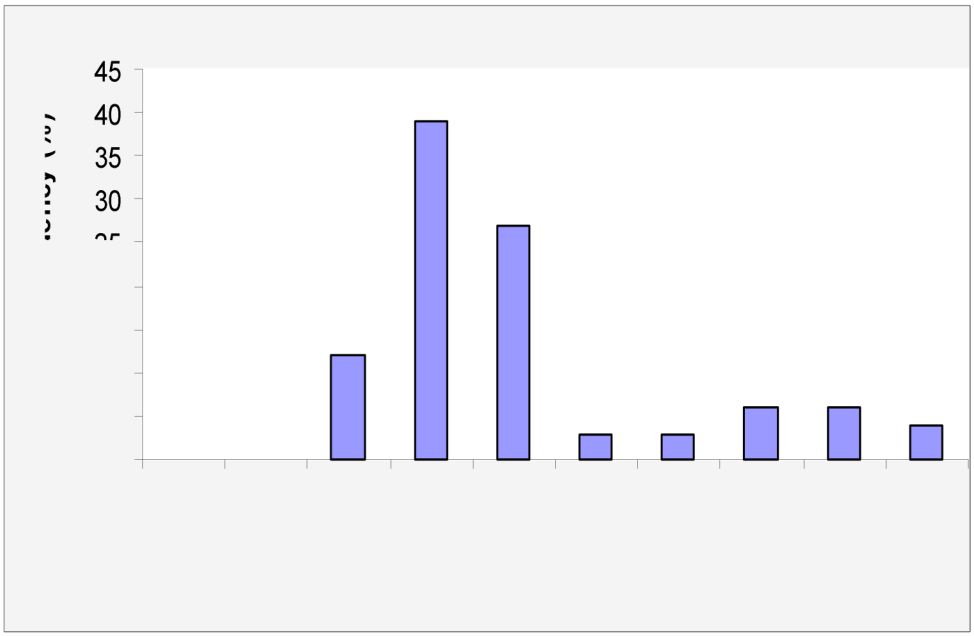


Figure 23: Histogram of particle size distribution for Polyvinylpyrrolidone Microcapsule (1:4 ratios)

S.N	Type of polymer	Ratio Drug: Polymer	Length Diameter (Mean) Micrometer	Surface number (Mean) Micrometer	Volume number (Mean) Micrometer	Volume surface (Mean) Micrometer
1	Ethylcellulose	1:1	194.00	204.63	213.72	233.13
2	-do-	1:2	133.50	151.90	168.82	201.54
3	-do-	1:3	316.50	354.54	383.05	447.42
4	PVP	1:2	248.00	261.58	273.46	298.86
5	-do-	1:3	276.00	293.21	310.08	346.80
6	-do-	1:4	229.00	247.43	267.35	312.13

Average Particle size of Microcapsules

Table 25: Average particle size of microcapsules with different drug to polymer ratio.

In the above table it clearly shows that the average particle size of the microcapsules increases with decrease in the drug to polymer ratio except 1:2 ratio. Similarly specific surface area decreases in the same manner.

7.7 DRUG-EXCIPIENT COMPATIBILITY STUDY BY FT-IR ANALYSIS

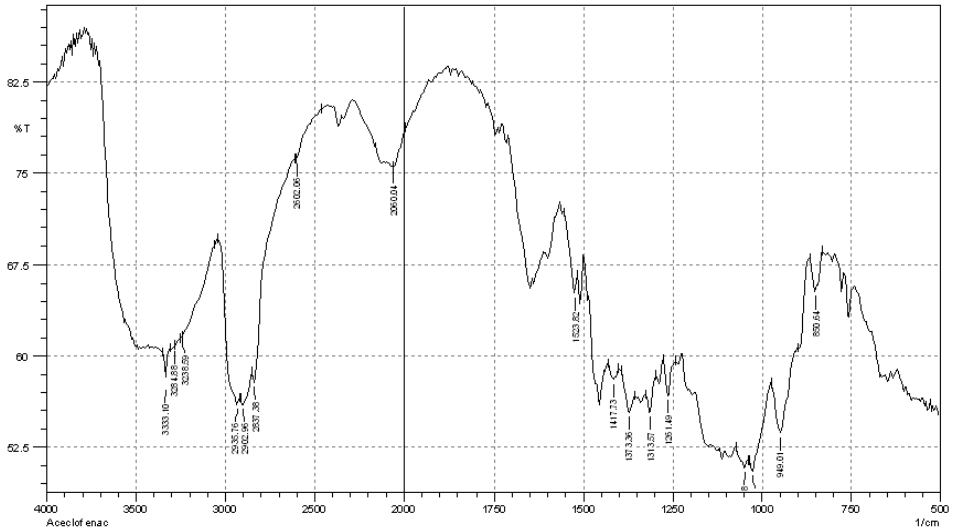


Fig. 24: IR SPECTRA OF ACECLOFENAC WITH MAJOR PEAKS AT 3333.10, 2935.76, 1770.56, 1523.82, 1313.57, 850.64

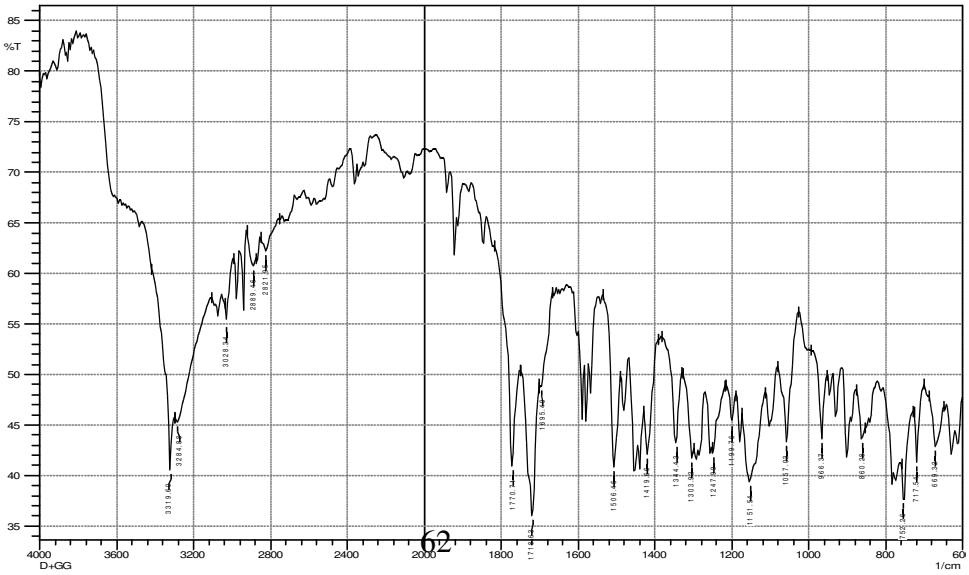


Fig. 25: IR SPECTRA OF PHYSICAL ADMIXTURE-1 WITH MAJOR PEAKS OF ACECLOFENAC AT 3319.60, 2938.40, 1770.71, 1504.46, 1303.92, 860.28

***Physical admixture-1 = Aceclofenac + Ethyl Cellulose**

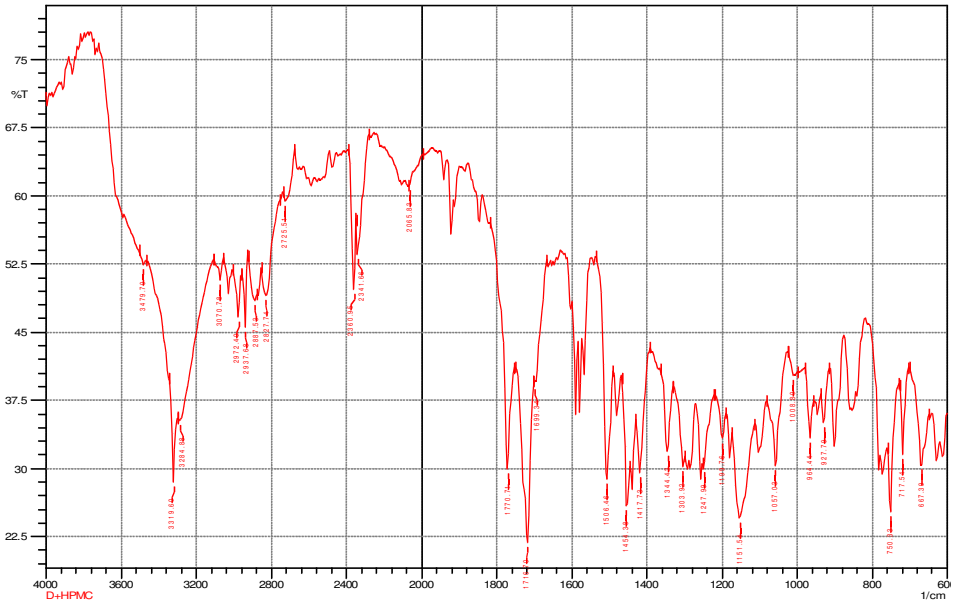


Fig. 26: IR SPECTRA OF PHYSICAL ADMIXTURE-2 WITH MAJOR PEAKS OF ACECLOFENAC AT 3319.60, 2937.68, 1770.71, 1506.46, 1303.92, 850.64

***Physical admixture-2 = Aceclofenac + PVP**

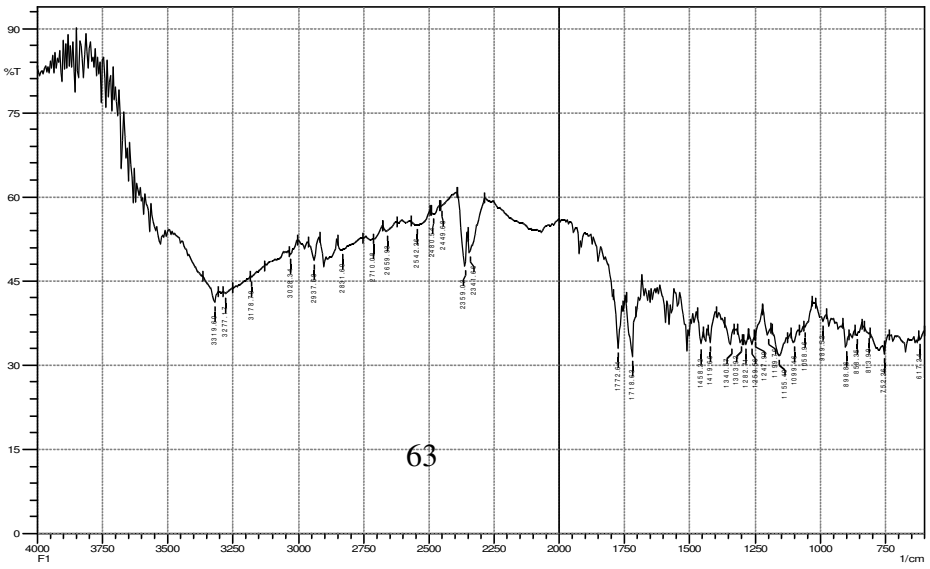


Fig. 27: IR SPECTRA OF FORMULATION WITH MAJOR PEAKS OF ACECLOFENAC AT 3319.60, 2937.68, 1772.64, 1511.21, 1303.92, 858.35

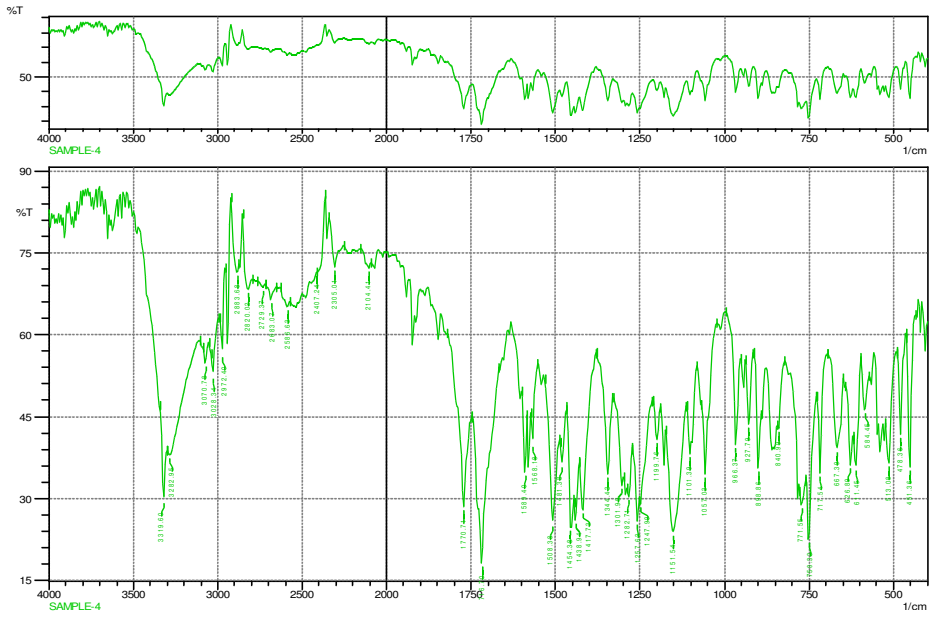


Fig. 28: IR SPECTRA OF FORMULATION WITH MAJOR PEAKS OF ACECLOFENAC AT 3319.60, 2932.40, 1770.71, 1503.38, 1301.99, 840.99

Drug-Excipient compatibility was carried out by FT-IR analysis. Initially the IR spectrum of pure drug was obtained. After that various admixtures of drug with other excipients like Ethyl cellulose, Poly vinyl pyrrolidone and Formulations were prepared and IR Spectra were obtained. The obtained spectra of physical admixtures and formulations were observed for major peaks of drugs. The results of this

observation were concluded that there is no interaction between the drug (Aceclofenac) and other excipients**.**

8. SUMMARY AND CONCLUSION

Microencapsulation has received considerable attention in pharmaceutical and biomedical application, specifically achieving sustained release and controlled release objectives. Thus it is an useful method for prolonging drug release from dosage forms, reducing adverse effects and to deliver drugs in a controlled manner.

In the present study, the drug, Aceclofenac is microencapsulated to prolong its action in the form of microcapsules and to explore, which polymer is suitable for this purpose. Therefore, two different polymers with similar physicochemical properties are chosen and used for the micro encapsulation with same procedure.

Preparation:

Solvent evaporation method may be used as a simple and common method to prepare Aceclofenac sustained release microcapsules with different polymers.

When acetone is used as a solvent for the polymeric internal phase, the ethyl cellulose is able to encapsulate and it is failed, when dichloromethane is used as a solvent. The expected reason for the failure of micro encapsulation with dichloromethane is may be due to difference in volatility between the two solvents. The drug is effectively encapsulated with polyvinylpyrrolidone, when the external phase containing liquid paraffin.

The selection of best polymer is based on the observation of the following four results of evaluation of microcapsules.

Encapsulation efficiency: Ethyl cellulose is able to microencapsulate the drug, when its concentration is between (5-15) %w/v in solvent acetone, whereas PVP polymer is able to micro encapsulate, when its concentration is 10 % w/v or more in acetone.

Encapsulation efficiency of ethyl cellulose microcapsules with 1:1 drug to polymer ratio is 96.01%, with 1:2 ratio is 94.45% and with 1:3 ratio is 80.40%. Since the encapsulation efficiency decreases with increase in the ratio, it can be considered that 1:1 ratio is the comparatively good ratio. Similarly, encapsulation efficiency of PVP microcapsules with 1:2 ratio is 92.50%, with 1:3 ratio is 60.10% and with 1:4 ratio 46.44%. In this case 1:2 ratio also showed good encapsulation efficiency than 1:3 and 1:4 ratios. So it can be considered as an optimum ratio.

The amount of drug loaded and the encapsulation efficiency of microcapsules prepared under various formulation conditions are depicted in formulation table.

As expected, increasing the amount of polymer in drug : polymer ratio and increasing the polymer concentration in internal phase caused a decrease in the drug content in microcapsules in both cases.

It seems that, increasing the drug: polymer ratio more than 1: 4 in polymeric solution leads to higher internal phase viscosity, which in turn results in the formation of larger particles. It should be mentioned that, microcapsules formation was found to be impossible, probably due to high viscosity of drug: polymer solution prepared at the ratio of more than 1: 4 and dispersibililty of internal phase into continuous phase.

Dissolution Profile:

Ethylcellulose and Polyvinylpyrrolidone (PVP) microcapsule reduces the inherent dissolution rate of the pure drug by about 16 times *i.e.* the time taken to dissolve 90 % of the pure drug is 45 minutes and it is increased to 11-12 hrs in case of Ethylcellulose microcapsule and to 11-13 hrs in case of Polyvinylpyrrolidone microcapsule.

It was observed that the release kinetics of ethyl cellulose and poly vinyl pyrrolidone microcapsules have got a good correlation with the Higuchi model. The results indicated that, various drug : polymer ratios in microcapsule preparation did not change the release kinetics.

The time taken for 90 % release of the drug from ethylcellulose microcapsules with 1:1 drug-polymer ratio was 11.85 hrs, with 1:2 ratio was 10.90 hrs, while, with 1:3 ratio was 11.18 hrs. Therefore, decrease in dissolution rate of different drug to polymer ratio was of the following order: 1:2 > 1:3 > 1:1. Similarly the time taken for 90% release of the drug from PVP microcapsule with 1:2 drug to polymer ratio was 11.51 hrs, with 1:3 ratio was 12.61 hrs while, with 1:4 ratio was 12.35 hrs. Therefore, decrease in dissolution rate of different drug to polymer ratio was of the following order: 1:2 > 1:4 > 1:3.

The possible expected result for this release profile with both the polymers was mainly focused on the difference in particle size between the ratios of the same polymer. As it was observed that the diameter-volume-surface for ethyl cellulose microcapsule with 1:1 drug to polymer ratio was 233.13 µm, with 1:2 ratio was 201.54 µm and with 1:3 ratio was 447.42 µm. So, specific surface area was 1:2 > 1:1 > 1:3. Similarly, diameter-volume-surface for PVP microcapsule with 1:2 drug to polymer ratio was 298.86 µm, with 1:3 ratio was 346.80 µm and with 1:4 ratio was 312.13µm. So, specific surface area was 1:2 > 1:4 > 1:3 and hence the drug release rate follows the same order of release.

Particle size analysis: It was observed the mean particle size of the microcapsule increase with increase in polymer concentration, but increasing the stirring speed resulted in a decrease in the mean particle size of microcapsules.
Histogram shows that, ethyl cellulose microcapsules with drug to polymer ratio 1:1 and 1:2 are uniform in size and shape with narrow range of distribution, whereas, PVP microcapsules are irregular shapes with wide range of size distribution.

FTIR study: Under IR study the functional group and finger print region, all the peaks of the drug, polymer and drug loaded microcapsules were correlated with each other.
Thus, from the figure it is observed that, there was no significant difference in the IR spectra of pure aceclofenac and drug loaded microcapsules. The characteristic N-H stretching of secondary amine, C-H stretching of pure drug was unchanged in case of microcapsules. The results suggest drug stability during the encapsulation process.

In view of the project work, it is concluded that Microencapsulation of Aceclofenac drug with Ethylcellulose in 1:1 ratio may be considered as best form for drug delivery in terms of release profile, encapsulation efficiency and particle size distribution.

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